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I. SOME REMARKS ON THE USE OF MALLORY'S PHOSPHOTUNGSTIC ACID HÆMATOXYLIN, AND A NOTE ON THE MUSCULUS PAPILLÆ OPTICI OF NIKOLAÏ.

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PHOSPHOTUNGSTIC acid hæmatoxylin was brought forward by Mallory* as a differential stain for the neuroglia of the central nervous system, for which purpose it is probably unexcelled. During the past three years the writer has made extensive use of it in staining sections of the eye, and has found it of great value, not alone for neuroglia, but for other tissues as well. It was found, however, that the method of fixation, recommended by Mallory for the central nervous system, was of little service for the neuroglia of the eye, and that in the case of other tissues the results obtained varied with the method of fixation employed. The stain itself, as given by Mallory, is as follows:—

Hæmatoxylin	0·1
Water	80
10 per cent. aqueous solution of phosphotungstic acid (Merck)	20
Peroxide of hydrogen (U.S.P.)	2

* Journal of Experimental Medicine, 1897, p. 532; *ibid.*, 1900, p. 15.

"Dissolve the hæmatoxylin in a little water by the aid of heat and add it, after cooling, to the rest of the water and the acid. The solution keeps perfectly and can be used repeatedly."

This solution, even when used alone, gives excellent results, but, according to Mallory, these are not permanent, and he, therefore, advises the use of an alcoholic solution of ferric chloride to fix the stain. The latter solution removes the pink colour from the connective tissue, or, if the staining solution is old, converts it into a brown colour. The connective tissue, however, may be readily stained again by acid fuchsin alone or by van Gieson's stain. In fact, the writer has found this the best method of using van Gieson's stain for tissues fixed in Zenker's fluid or alcohol. The method of staining sections is given below. Lugol's solution, followed by alcohol, is, of course, to be used only for specimens fixed in Zenker's fluid. If the sections are overstained, the excess of stain can be removed by prolonging the treatment with the ferric chloride solution:

(1) Lugol's solution, 5 minutes.

(2) 95 per cent. alcohol until yellow colour is removed.

(3) Water (to remove alcohol).

(4) Phosphotungstic acid hæmatoxylin, 24 hours or longer.

(5) Wash quickly in water.

(6) 30 per cent. alcoholic solution of ferric chloride, 5 minutes.

(7) Wash in two or three changes of water.

(8) 2 per cent. acid fuchsin or van Gieson's stain, 5 minutes or longer.

(9) 95 per cent. alcohol, two changes.

(10) Ol. origanum cretici.

(11) Xylol balsam.

As just stated, the method of fixation recommended by Mallory does not give successful results in the case of the eye. The fixation methods found most useful by the writer are as follows:—

(1) *Formaldehyde 4 Per Cent., Four Days or Longer.*— Sometimes this gives beautiful results with the neuroglia of the optic nerve and retina, but more often that of the latter fails to strain. Why Müller's fibres should stain intensely in some specimens and remain colourless in others that have been subjected to the same treatment, is difficult to understand. A striking as well as a constant staining reaction after this method, however, is exhibited by the rods and cones, the inner limbs of which always take a strong blue colour, while the outer limbs usually do not stain. Not infrequently the nuclei and fibrils of the rods and cones also stain intensely. This produces a remarkable differentiation between the outer and inner nuclear layers, the latter remaining unstained. The contrast between the two layers may be further heightened by staining 24 hours in lithium carmine after differentiating in the ferric chloride solution. The elements of the internal nuclear layer then take the carmine stain. In some specimens only portions of the retina show this differentiation. It seems to occur most often in cases of separation of the retina or choroiditis, where, of course, the nourishment furnished the retina by the choriocapillaris is interfered with, but it also occurs in apparently normal retinæ. The condition is present also in the retina of the guinea pig and in that of the frog. In the one specimen of the retina of a rabbit, upon which the stain was tried, neither of the two nuclear layers took the stain, but the rods and cones were stained as in the human retina.

These staining reactions seem to show very conclusively that the rods and cones, as well as their nuclei and fibrils, differ essentially from the bipolar cells of the retina. It is not safe, however, to conclude that they are similar in nature to neuroglia. Under any circumstances phosphotungstic acid hæmotoxylin is not such a strictly differential stain as to prove that any substance coloured by it is neuroglia. It is differential, however, in the sense that it distinguishes neuroglia fibrils (not cells) from all other fibrils for which

they are likely to be mistaken. More than this cannot be expected of any so-called differential stain.

Formaldehyde fixation also gives other interesting results with this stain. It is the best method for demonstrating fibrin, for although fibrin itself stains after the other methods of fixation, by this method it is brought out in sharper contrast with the surrounding tissue. The nuclei of normal tissues generally stain feebly or not at all. This is the case also with the nuclei and cells of glioma retinæ. Sarcoma cells as a rule stain deeply, the nucleoli and nuclear membranes being especially well brought out. The nucleoli stain perfectly black, and in some cases are the only parts of the cell to take the stain. The nuclei of cells in an early stage of degeneration stain intensely black. After this method, peculiar markings are brought out in medullated peripheral nerves. These were noted by Mallory after his special method of fixation, but are much more sharply defined after fixation in formaldehyde alone. They appear (Fig. 2) as a series of arrow heads, attached to a central core, all pointing in the same direction. They always stain intensely black, even in sections in which neuroglia fails to stain. The writer has found them present in plexiform neuroma of the eye-lids, and they are therefore of some importance from a diagnostic standpoint. The markings apparently correspond in position to the lines of junction of the Schmidt-Lantermanns segments, and it seems not unlikely that they are due to collections of neurokeratin.

(2) *Formaldehyde* 4 *Per Cent.*, 4–10 *Days;* 10 *Per Cent. Nitric Acid*, 48 *Hours; Running Water*, 24 *Hours.*—This is the best method for the neuroglia of the eye, and is practically always successful. The writer has found it also equally as satisfactory for the brain and spinal cord as Mallory's more elaborate method. Müller's fibres are more apt to stain poorly than the neuroglia fibrils of the optic nerve. This is probably due to the fact that the former really consist of the bodies of neuroglia cells. As a rule, better results seem to be obtained with pathological than with

normal retinæ. Separated retinæ yield particularly good specimens, and beautiful specimens can also be obtained showing the proliferation of neuroglia in phthisis bulbi and atrophy of the retina (Fig. 3). The writer has applied it to a number of cases of glioma retinæ with and without rosette formations, but has never been able to find neuroglia fibres which could be regarded as belonging to the tumours themselves.* Neuroglia fibres, however, are sometimes to be found extending out from a portion of retina that has been incorporated in the tumour. Since fibrin and certain products of necrosis stain blue by this method, care must be used not to mistake them for neuroglia. The nuclei of normal cells also stain, so that phosphotungstic acid hæmatoxylin may be used to advantage as a nuclear stain for any part of tissue that has been decalcified by nitric acid.

(3) *Zenker's Fluid*, 24 *Hours*; *Running Water*, 24 *Hours*.—Before placing the globe in this fluid it should be sectioned without freezing in a vertical plane anterior to the ora serrata. Since the retina is attached at the latter situation, air cannot make its way behind it, and it does not become separated. Of course it may later become separated during the steps preliminary to embedding. This is the best method of fixation for general purposes, although alcohol gives results almost as satisfactory. The cells of normal tissues, tumour cells, and the various cells of inflammation, are all perfectly stained. Elastic tissue stains brown, smooth muscle stains deep blue, and is thus sharply differentiated from connective tissue, which is stained bright red by the acid fuchsin. Mallory states that "smooth muscle fibres sometimes stain after Zenker's fluid, but the results are not constant." This probably applies only to tissues obtained at autopsy, which, of course, cannot always be free from post-mortem changes. In the case of enucleated eyes, however, this difficulty is not met with. Possibly also the staining would not be constant throughout a large piece of tissue,

* Specimens fixed by Mallory's method also fail to show neuroglia fibres in these tumours.

but this again is not a difficulty in the case of the eye. At any rate the writer has never known the method to fail to stain the smooth muscle of the eye, including that of its blood vessels. The dilator fibres of the iris, the nature of which has been much discussed, are deeply stained and their structure so well preserved as to leave no doubt that they are smooth muscle fibres. The fibres of peripheral nerves are well stained, but the peculiar arrow-head markings, mentioned above, are absent.

The retina is stained in a beautiful manner after Zenker's fluid, the rods and cones being brought out especially well. This is due, however, as much to the method of fixation as it is to the stain. The inner limbs of the rods and cones are stained blue, the cone ellipsoid staining more deeply than the other portions of the cones. The outer limbs of the rods and cones appear as transparent hollow tubes, whose walls take a blue tint. In case of the cones the membrane forming the walls of the outer limbs is continued over the inner limbs also. Attached to the inner surfaces of the walls of the outer limbs are to be seen numerous granular particles stained slightly red. When acid fuchsin is not used, they stain blue. Sometimes the granules completely fill the outer limbs, or occasionally four or five globular masses make up their contents. At the junction of the inner and outer limbs of a cone there is always a clear unstained zone, which in the short thick cones usually takes the form of a bulbous expansion. Here and there between the rods and cones there is a transparent substance stained red. In places large globules of this material are seen, suggesting that it is the remains of an interstitial substance which has been for the most part dissolved out.

When the nucleus of a cone is situated outside the limiting membrane, as it occasionally is, there is usually a clear crescent-shaped space just ahead of it, suggesting that the nucleus is situated in a vacuole which it does not quite fill. In the specimens of the writer, there seem to be two distinct classes of nuclei situated outside the limiting mem-

brane (vorgelagerte Körner, Greeff). In one class the nuclei always have the clear crescent spaces ahead of them, and are not limited to any special part of the retina, while in the other the crescents are absent and the cones are short and thick. The interesting feature of the second class, however, is the fact that they always occur behind a vessel so large that the retinal layers behind it, as well as the limiting membrane, are curved outward and the rods and cones much shortened (Fig. 4). The displacement of the nuclei in the second class then seems to be brought about by pressure of blood vessels. It is less likely that it could be due to atrophy resulting from the inability of the cones behind the vessels to carry out their functions.

The external limiting membrane of the retina stains deep blue, the hyaloid membrane reddish-brown. Neuroglia fibres in both the retina and optic nerve are well stained, but are not so sharply differentiated from the nervous elements as by the foregoing method. However, this method has the advantage over the latter of being constant in its results and of preserving neuroglia cells and nuclei more perfectly. In glioma retinæ by this method also the writer has always failed to find anything resembling neuroglia fibres in the tumour proper. But the cells and nuclei of these tumours, the limiting membrane of the rosettes, with the little projections through it (rudimentary rods and cones) are most perfectly brought out.*

Note on the Musculus Papillæ Optici of Nikolaï.

The cells in the optic disc, recently described by Nikolaï† as forming a musculus papillæ optici, are deeply stained by

* Mallory's connective tissue-stain also gives interesting results after Zenker's fluid when applied to the retina. It is particularly useful for demonstrating the blood-vessels, the walls of which are stained bright blue. The inner limbs of the rods and cones stain dark red, the walls of the outer limbs blue, and the contents of the latter, orange. The interstitial substance mentioned above stains blue. The external limiting membrane stains red, the hyaloid membrane intensely blue. Müller's fibres and nerve fibres stain red. All nuclei stain orange.

† Annales D'Oculistique, Nov., 1902, p. 342.

the last-mentioned method, and their structure so well brought out as to render the view that they are smooth muscle fibres improbable. Some of these elements appear in the form of long spindle cells with double contours, having rod-shaped nuclei, and certainly bear a close resemblance to smooth muscle. When they lie entirely in the plane of the section, however, they can be seen to terminate in fibrils longer than those ordinarily forming the extremities of smooth muscle fibres. Mixed in with these cells are to be seen shorter cells which break up into one or more fibrils at each end. In fact there are all gradations to be met with between spindle cells with one fibril at each end to stellate cells (not "spider" cells) with several fibrils attached. Some of the cells have scarcely any cell body, and the fibrils are given off almost at the nucleus. Many of the stellate cells are similar in shape to the cells of myxomatous tissue or to the cells of the iris stroma, but differ from them in that the processes (fibrils) of the cells in the disc do not branch and do not unite with the processes of neighbouring cells. In specimens stained by the ordinary methods, it is difficult to make out the fibrils, or at least their relationship to the cells, and the spindle cells cannot be distinguished from smooth muscle fibres. In any case, many of the fibrils are missed because they pass out of the plane of the section.

The only real evidence advanced by Nikolaï, which goes to show that the spindle cells are smooth muscle fibres, is based on morphology. This seems insufficient when it is considered that the cells in question occur in a structure in which there is no physiological indication for the presence of muscle fibres. Moreover, Nikolaï fails to exclude the possibility, which seems most probable, that they are neuroglia cells. It is true that he applied Weigert's stain and obtained negative results, but he overlooked the fact that by this stain only the fibrils and not the cell bodies of neuroglia are stained. So far as the writer is aware, there is no stain which will clearly differentiate neuroglia cells from smooth muscle fibres.

The stellate cells, as well as the other cells with fibrils attached, of course cannot be regarded as smooth muscle fibres, and since the fibrils of the spindle cells are entirely similar to those belonging to the other cells of the disc, it is reasonable to suppose that all of these cells are of the same nature, and that the spindle cells, too, are not smooth muscle fibres. An additional argument in favour of this view is the fact that the writer has seen, under pathological conditions, marked proliferation of the cells of the disc with the production of many new spindle cells possessing fibrils.

But if the cells and fibrils of the disc, including the spindle cells, are neuroglia elements, they differ from the neuroglia found in the retina and optic nerve proper, and from that in the brain and spinal cord. As is well known, it is a matter of dispute as to whether or not neuroglia fibres in the central nervous system are the processes of cells, Weigert* vigorously upholding the negative side of the question. It has been claimed that the neuroglia fibrils pass through the cells unchanged. In the trunk of the optic nerve, the writer has not been able to convince himself that the fibrils are in continuity with cells, although some of the cells certainly have short processes. It is also difficult to determine whether the fibrils pass through the cells or simply run along their sides. Here, too, one of the arguments, advanced in case of the central nervous system, seems to hold good, namely, that the fibrils are too numerous and the cells too few for each fibril to be connected with a cell. At the lamina cribrosa, however, the character of the neuroglia rather abruptly changes, the fibrils become coarser and much less numerous, and, in fact, seem identical with the fibrils attached to the cells described by Nikolaï. Moreover, the cells in the disc are sufficiently numerous to substantiate the view that each fibril is attached to a cell. The fibrils in the optic disc differ also as regards staining properties from those in the nerve trunk, for after fixation

* Beiträge zur Kenntnis der normalen menschlicher Neuroglia. Frankfurt-a-M., 1895.

in formaldehyde alone or even when followed by nitric acid, they sometimes fail to stain in specimens in which the fibrils of the nerve trunk stain deeply.

On the other hand, the writer has found the same kind of cells and fibrils, including the spindle cells, in a true glioma of the brain, and in cases of phthisis bulbi, such cells were found to make up a large part of the new-formed neuroglia arising from the retina. They also occur in the retina under other pathological conditions. It would seem, therefore, that the spindle cells in the optic disc, as well as the other cells with fibrils attached, are really neuroglia elements, but that they represent a less highly differentiated form of neuroglia than that in the optic nerve proper.* And it seems more than probable that the spindle cells are modified spongioblasts, and are closely related to Müller's fibres. This view is borne out by the fact that in the retina just posterior to the ora serrata, there are frequently to be found spindle cells similar to those in the disc. It is also consistent with the fact that the cells in question occur at the point of transition between the optic nerve and retina.

Description of Plate.

1. Separated retina, showing Müller's fibres. Formaldehyde fixation.

2. Arrow-head markings in medullated nerves. From a case of plexiform neuroma of the eye-lid. Formaldehyde fixation.

3. Proliferation of neuroglia in atrophied retina (gliosis retinæ). Formaldehyde fixation, followed by nitric acid.

4. Normal retina, showing shortened cones behind blood-vessel with nuclei external to membrana limitans externa. There is another vessel on the left. Fixation in Zenker's fluid.

* The question of the occurrence of differentiated and undifferentiated neuroglia fibres in gliomata of the brain has been discussed by E. W. Taylor, Journal of Experimental Medicine, 1897, p. 611.

FIG. 1.

FIG. 2.

FIG. 3.

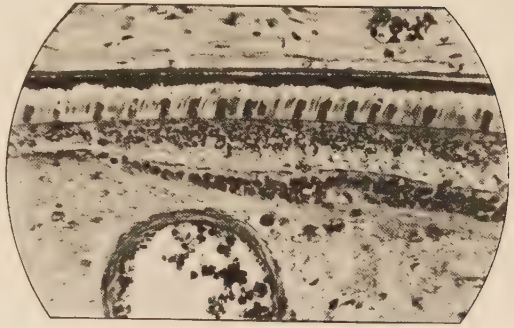

FIG. 4.

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II. A HITHERTO UNDESCRIBED MEMBRANE OF THE EYE, AND ITS SIGNIFICANCE.

While studying the external limiting membrane of the retina in a section of a normal eye, the writer was surprised to find it continue on at the margin of the disc and pass into the layer of pigment epithelium, where it could be followed, until the gradually increasing pigmentation hid it from view. Other sections of the same eye, bleached by the method of Alfieri,* and stained in a variety of ways, showed the still more surprising fact that this membrane was present in the pigment layer throughout the fundus. The eye from which the specimens were obtained was removed from a man aged 65 years, who suffered from extensive carcinoma of the eye-lid with probable involvement of the orbit. It was opened immediately after enucleation and fixed in Zenker's fluid. The writer has since found the membrane in eyes fixed in formaldehyde, but in these the pigment layer is not so well preserved. A few sections from an eye fixed in formaldehyde and containing a glioma retinæ were particularly fortunate. They passed through a portion of the pigment layer in which the pigment was almost entirely absent, and therefore did not require bleaching. Mallory's[2] phosphotungstic acid hæmatoxylin seems to be the best stain for the membrane, because in specimens fixed in formaldehyde, and in bleached specimens fixed in Zenker's fluid, it does not stain the cells to any extent, and the membrane is brought out in sharp contrast. The ordinary alum hæmatoxylin and eosin method of staining, however, gives fairly satisfactory results, the membrane taking the eosin stain.

* Celloidin sections are placed in a solution of permanganate of potash, 1 : 2000, for 24 hours, and then in oxalic acid, 1 : 300, for a few hours. The permanganate solution should be made up fresh each time, and a large volume of it should be used. If the bleaching is not complete, the process can be repeated.[1]

The appearance presented by this membrane in cross sections is that of a delicate line running along near the inner margins of the cells. The latter project beyond it in the form of processes of variable length, showing from this fact alone that the line does not represent the inner contours of the cells. Occurring at almost regular intervals on the line, there are black dots, each of which on close examination is found to be situated at the line of junction of two cells. On careful focusing it can be seen that the line is not always on the same level, evidently passing sometimes behind and sometimes in front of the cells ; rarely it is missed entirely for a cell or two. This makes it difficult to obtain a good photograph of the membrane. In oblique sections the true structure of the membrane is at once apparent, the latter appearing then not in the form of a straight line, but in a series of hexagonal loops, which are fused together at their sides of contact so as to form a screen into the openings of which the pigment cells project. The little dots resolve themselves into the sides of the loops, which in cross-section had pointed more or less directly at the observer. Fig. 1 shows the membrane in both cross and oblique section.

That this is a true fenestrated membrane, and is not an appearance produced by the contours of the cells, there can be no doubt whatever. In the first place, as just stated, it does not correspond in position to the margins of the cells. Secondly, in phosphotungstic acid hæmatoxylin followed by acid fuchsin it stains blue, whereas the cells stain pink, or not at all, and show no vertical blue lines between them. Thirdly, in certain places where two neighbouring cells have shrunken apart, it remains intact. Fourthly, it can frequently be seen projecting beyond a fragmented portion of the pigment layer. Such a projection in cross section is shown in the photograph, Fig. 2. The writer has also not infrequently seen, even in unbleached specimens, horizontal loops out of which the cells had fallen, which were still in continuity with the loops of adjoining cells, Fig. 3.

Moreover, this membrane has nothing whatever to do

with the cement substance or neurokeratin envelope that has been described as lying between or covering over the cells of the pigment layer. While there is no reason to doubt that such a substance exists, it does not stain in the specimens of the writer. However, on carefully focusing, a bright line or space can be made out between the cells, which in some instances is especially plain. The reason it cannot always be seen with the same distinctness is probably due to the fact that the cells are hexagonal in shape.

As already mentioned, in phosphotungstic acid hæmatoxylin the membrane stains blue in both bleached and unbleached specimens. In the specimens from the case of glioma retinæ which required no bleaching, the neuroglia of the optic nerve, Müller's fibres of the retina, the rods and cones, and the external limiting membrane, were also stained. In bleached specimens of the normal eye fixed in Zenker's fluid, the only other structures to take the stain were the external limiting membrane, and a large number of neuroglia fibrils in the optic nerve. Neither membrane stained by Weigert's elastic tissue stain. Mallory's connective tissue stain[2] could be applied of course only to unbleached specimens fixed in Zenker's fluid, and in these the visible part of the membrane in the pigment layer and the external limiting membrane were stained a deep red. Staining reactions, therefore, seem to offer strong evidence that both of the membranes consist of a substance identical with or closely allied to neuroglia.

Not only does the membrane of the pigment layer stain in the same way as the membrana limitans externa, but it has also the same structure. The component loops of the latter membrane are of course smaller, since they surround smaller structures, but although the loops for the rods are particularly small, each rod as well as each cone has its individual loop. For this reason the dots seen along the membrane in cross section occur at much more frequent intervals than in the case of the membrane of the pigment layer. The small size of the loops makes it difficult to determine their exact shape, but in general they seem to be round. However,

at a short distance from the optic disc, where the rods and cones assume the form of short thick processes, the loops are unmistakably hexagonal in shape.

Another fact of importance, which indicates that the two membranes are really identical structures, has already been mentioned, namely, that in some places at least they are continuous at the margin of the disc. This can be explained in one or both of two ways. It could be the result of the actual continuity of the pigment layer with the invaginated portion of the optic stalk during early embryonal life, or it could be due to the fusion of the two layers at the disc, and the consequent fusion of the membranes. The specimens of the writer seem to indicate that the former is the correct explanation.

The writer has a few specimens which show a similar membrane in the ependymal epithelium of the brain and spinal cord. Possibly this has already been described by others.

For years the external limiting membrane of the retina has been described as being formed either by the apposition of the outer ends of Müller's fibres or by lateral interlacing offshoots from them. Greeff[3] in his elaborate article on the retina still holds to this view. For a long time also it was thought that in a similar way Müller's fibres formed an internal limiting membrane, but this view has now been generally abandoned. There is of course a membrane, the hyaloid membrane, lining the inner surface of the retina, but it is in no way similar to the membrana limitans externa. It stains slightly in Weigert's elastic tissue stain, and intensely in Mallory's connective tissue stain, and is, therefore, evidently of mesoblastic origin. The basis for the belief that the membrana limitans externa is formed by Müller's fibres seems to rest on the fact that the latter have been seen apparently to end in contact with it. In view of the fact, however, that an entirely similar membrane, and one with which it is directly continuous, exists in the pigment layer where there are no such fibres, the writer feels that this theory also must be abandoned. Moreover, although the writer has carefully studied many

sections in which Müller's fibres were deeply stained by phosphotungstic acid hæmatoxylin, in no instance, at least in the normal fundus of the adult, were they found to end in contact with the membrana limitans externa. The little processes that have been described as arising from the membrane and passing in between the rods and cones so as to isolate them, are evidently nothing but the cut ends of loops seen obliquely.*

No one can doubt that the membrane in the pigment layer is a product of the cells which project through it. It seems clear, therefore, that the membrana limitans externa must have a similar origin. The latter membrane, however, makes its appearance long before the rods and cones are formed, so that it must be manufactured by cells which later become converted into these elements. The natural deduction from these conclusions is that the rods and cones, and the cells of the pigment layer, are essentially of the same nature, and that the former are really only modified spongioblasts (of His). Two facts already mentioned support this deduction, one is that at the margin of the optic disc the rods and cones can sometimes be seen gradually to assume the character of the pigment cells, and the other is that the membrana limitans externa has the characteristic staining reactions of neuroglia. In the preceding article, too, it was pointed out that the rods and cones, and frequently also their nuclei and fibrils, could be differentiated from the bipolar cells of the retina by the neuroglia stain. The theory that the rods and cones represent modified ependymal cells is not new,† but it seems to the writer that the foregoing considerations make this theory practically a certainty. It is interesting that this supports Barker's[5] contention, based on analogy, that the rods

* The appearance of little processes is also sometimes produced by the contours (membranes) of the cones, which are especially distinct near the membrana limitans externa. They are also to be seen running inwards, and may be mistaken for fine branches of Müller's fibres.

† W. Krause[4] regards the rods and cones as ependymal cells with their cilia matted together.

and cones are not nervous elements, but sensory epithelium, and that the bipolar cells of the retina correspond to the cells of spinal ganglia.

As is well known, in the rosettes of glioma retinæ there is a membrane which on cross section appears to be identical with the membrana limitans externa of the retina. So far as the writer can ascertain, however, its appearance in plane section has never been described. To determine the structure of this membrane, a glioma retinæ was selected in which rosettes were both unusually large and numerous. The globe had been opened immediately after enucleation and portions of the tumour fixed in Zenker's fluid, formaldehyde, and alcohol respectively, but Zenker's fluid was found to give by far the most satisfactory results. Sections from the portion of the tumour fixed in this fluid, show conclusively that the membrane of the rosettes is a fenestrated structure similar in every way to the membrana limitans externa and to the membrane of the pigment layer. The same stains were applied as in the case of the other two membranes and with identical results. In these specimens the fenestrated structure can be made out in the great majority of the rosettes, but in some of them it is especially distinct. Fig. 4 shows a rosette in the upper part of which the membrane is cut transversely, while below it is cut in plane section and can be seen to become continuous with a series of loops. It is noteworthy that these loops are always hexagonal and of about the same size.

In the centres of many rosettes there are other hexagonal figures whose outlines are coarser than those of the true membrane. Such figures are also frequently seen elsewhere in the tumour. They can be easily distinguished from the membrane by means of Mallory's connective tissue stain, which stains their walls slightly blue, while the membrane is stained a deep red. This stain seems to show a definite intercellular substance throughout the tumour which takes a blue tint. It does not stain sufficiently blue, however, to indicate that it is a reticulum of connective tissue. The hexagonal figures in the centres of the rosettes, therefore, no doubt

represent the walls of spaces out of which cells have fallen.

The structure of the membrane in the rosettes explains why the latter assume their peculiar form, for it is evident that if a few cells became bound together by such a membrane, and they were otherwise unhampered in their growth, they would be compelled to form a more or less spherical body. If the free ends of the cells groups did not finally meet, a spiral figure would result, and just such spirals are frequently seen. The writer has also found single cells with a membrane on one end, as well as curved groups of several cells which were obviously the beginnings of rosettes. This explains very well why tumour cells are often seen within the cavity of rosettes, evidently being enclosed during the formation of the latter.

The similarity of the rosettes of glioma retinæ to the layer of rods and cones was first pointed out by Flexner[6] and a few years later by Wintersteiner.[7] Although the work of these two observers was unquestionably independent, their conclusions were almost identical. Each took the view that the rosettes indicated a tendency on the part of the tumours to form rods and cones, and each suggested the term neuroëpithelioma as the proper designation for these tumours. Flexner's conclusions were based upon the study of one case only, which he evidently considered to be of a different nature from the usual type of glioma retinæ. He also thought that he could locate its origin in the external nuclear layer of the retina. Wintersteiner,[8] on the other hand, studied a large number of cases, and came to the conclusion that the term neuroëpithelioma was applicable to them all, although most of them did not contain rosettes. The latter observer found also that these tumours probably started in the majority of cases from the internal nuclear layer.

A strong argument against the theory of Flexner and Wintersteiner in regard to the nature of rosettes, is the fact that according to accepted views the membrane of rosettes could not be formed in the same way as the membrana

limitans externa, since there is nothing corresponding to Müller's fibres in these bodies. Strangely enough, this fact seems to have been entirely overlooked. The observations of the writer, however, render this objection no longer valid, for it has just been shown that the membrana limitans externa is in all probability produced by the cells which go to form the rods and cones. It was pointed out, too, that the two membranes are identical in structure.

Sections of the tumour mentioned above, that was fixed in Zenker's fluid, show a closer resemblance between the rods and cones and the corresponding processes of rosettes than is realised. In some rosettes there are conical processes projecting beyond the membrane, the bodies of which stain deeply in phosphotungstic acid hæmatoxylin, and which terminate in unstained extremities. These processes in fact are indistinguishable from some of the thickened cones seen in a normal retina near the the optic disc and in the neighbourhood of the ora serrata. Moreover, the membrana limitans externa near the optic disc, as already noted, is made up of hexagonal loops as in the limiting membrane of rosettes. This shows, of course, that in both cases the cells are hexagonal in shape. It should not be overlooked that it is only here and there that one can expect to obtain a perfect longitudinal section of a rod or cone in spherical bodies like rosettes.

Flexner and Wintersteiner applied the term neuro-ëpithelioma to the tumours under discussion, because they regarded the latter as being composed of elements corresponding to the rods and cones, the neuroëpithelium of the retina. While, however, the latter name, first given by Schwalbe[9] to the rods and cones with their nuclei and fibrils, has met with general acceptance, no entirely satisfactory evidence has been brought forward to show that they are not really nervous elements. The observations of the writer, however, already given, strongly support the view that they are not nervous elements, but only slightly modified spongioblasts.

While then the nature of the rosettes in glioma retinæ seems plain, the character of the other elements in these tumours is still undetermined. Thus far there is no trustworthy evidence that the cells are differentiated into true ganglion cells or neuroglia cells. Greeff[10] claims that by means of the Golgi-Cajal method he has not only demonstrated several types of ganglion cells, but neuroglia cells as well. If ganglion cells can be found in cheese by this method, it is not surprising that they should have been found in a tissue so prone to undergo degeneration as is glioma retinæ. Then, too, the ganglion cells and neuroglia cells belonging to a portion of retina incorporated in the tumour might easily be mistaken for elements of the tumour itself. As stated in the preceding article, the writer has been unable to find neuroglia fibres in these tumours, which were not connected with the retina, by Mallory's method or by any of the modifications of this method there given. Brown Pusey[11] has recently described a case that he evidently regarded as glioma retinæ, and has arrived at the conclusion that glioma retinæ consists essentially of neuroglia elements. He also concluded that the limiting membrane of rosettes corresponded to the internal, not to the external, limiting membrane of the retina. Judging from the description of the case, however, the writer is very sure that it is really one of phthisis bulbi posterior following metastatic ophthalmitis, one of the conditions known clinically as pseudo-glioma. The "rosettes" were evidently nothing more than retinal folds.

In view of the fact, then, that there is no reason to believe that these tumours contain neuroglia, it is obvious that the term glioma retinæ is an inappropriate one. It is all the more so because there are tumours of the brain, termed gliomata, which are believed to be made up of neuroglia, and it seems possible that such tumours may yet be encountered in the retinæ. The term neuroëpithelioma, however, is no less inappropriate than the other. If it indicated no more than that the tumour took its origin from the epiblast of the neural

canal of the embryo, it would unquestionably be a most suitable term. Unfortunately, the term neuroëpithelium has been applied to the layer of rods and cones in the fully differentiated retina, and "neuroëpithelioma" therefore indicates a tumour whose essential elements correspond to the rods and cones. But, as a matter of fact, it is rare for rosettes to form more than an insignificant part of the tumour, and in most of these tumours they are entirely absent. It is possible, if not probable, that they simply represent a differentiation of the essential elements of the tumour, and that the latter may undergo differentiation in other directions as well. The possibility remains that many of the elements in these tumours are neuroblasts. It is evident, therefore, that "neuroëpithelioma retinæ" is a no more suitable designation than "glioma retinæ" for the tumours to which they have been applied, and that at present there is no reason why the latter should be supplanted by a term over which it has long priority.

Conclusions.

In the pigment layer of the retina there is a fenestrated membrane, identical in structure and staining reactions with membrana limitans externa.

The rods and cones are not nervous elements, but modified ependymal cells, and are analogous to sensory epithelium.

The limiting membrane of the rosettes of the glioma retinæ is a fenestrated membrane similar in every way to the membrana limitans externa, and the rosettes correspond to the neuroëpithelium of the normal retina.

The structure of the limiting membrane of rosettes explains why they assume their spherical and spiral-like forms.

"Neuroëpithelioma retinæ" is no more suitable than "glioma retinæ" for the class of tumours to which these terms have applied.

The writer desires to express his thanks to Mr. J. Herbert Parsons, to whom he is indebted for the microphotographs illustrating this and the previous article.

Fig. 1.

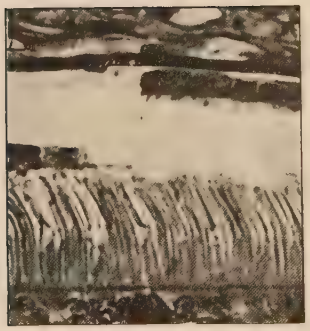

Fig. 2.

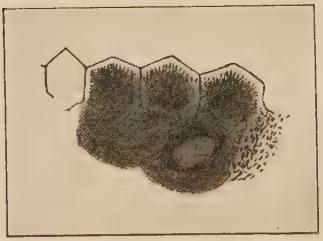

Fig. 3.

Fig. 4.

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References.

(1.) Alfieri. Monitore Zool. Ital., viii, 1897, p. 57. (Bolles Lee, The Microtomists' Vade Mecum, 1900, p. 328.).
(2.) Mallory. A Contribution to Staining Methods. Journal of Experimental Medicine, 1900, vol. v, p. 15.
(3.) Greeff. Die mikroscopische Anatomie des Sehnerven und der Netzhant. Handbuch der Augenheilkunde von Graefe-Saemisch, 1900, 2 Aufl. 20.
(4.) Krause, W. Uebersicht der Kenntnisse vom Bau der Retina im Jahre, 1895. Schmidt's Jahrb., Leipzig, 1896, p. 798.
(5.) Flexner. A Peculiar Glioma (Neuroëpithelioma?) of the Retina. Johns Hopkins Hospital Bulletin, 1891, p. 115.
(6.) Barker. The Nervous System, 1901, p. 541.
(7.) Wintersteiner. Über Bau, Wachstum und Genese des Glioma Retinæ. Wiener klinische Wochenschrift, No. 27, 1894, p. 493.
(8.) Wintersteiner. Das Neuroëpithelioma Retinæ, Franz Deuticke, 1897.
(9.) Schwalbe, J. Handbuch der Augenheilkunde von Graefe-Saemisch, 1 Aufl. 1.
(10.) Greeff. Der Bau und das Wesen des Glioma Retinæ. Deutsche medicinische Wochenschrift, 1896, Bd. 22, p. 327.
(11.) Brown Pusey. The Genesis of Glioma Retinæ in Neuroglia. Johns Hopkins Hospital Bulletin, 1902, p. 229.

Description of Plate.

1. Pigment epithelium with pigment removed, showing fenestrated membrane in both cross and oblique section.

2. Photomicrograph, showing a loop of the membrane in cross section extending beyond a fragmented portion of the pigment epithelium.

3. Isolated group of unbleached pigment cells lying transversely, showing hexagonal loop of membrane partially freed.

4. Rosette of glioma retinæ, showing limiting membrane in cross and plane section.

OBSERVATIONS ON RENAL RETINITIS.

By E. Nettleship.

(The following paper formed the introduction to a discussion on "Eye Changes in Relation to Renal Disease" at the meeting of the British Medical Association at Swansea on July 30, 1903. The paper is based chiefly on my records of all the cases—rather more than 100—that I have seen and noted, and the case numbers refer to these. The parts within rectangular brackets [ ] were either communicated to me by their authors after the paper was written, or formed part of the discussion.—E. N.)

Although much attention has been bestowed upon the retinal changes that occur in renal disease, information is still needed upon several points, from physicians and general practitioners as well as from ophthalmologists, and the following heads are suggested as containing material suitable for discussion:—

1. It is, of course, in the chronic interstitial and chronic parenchymatous forms of nephritis that albuminuric retinitis so commonly occurs. A few cases are recorded in connection with lardaceous disease, and with nephritis due to inflammation of the bladder, ureter, or pelvis of the kidney, but additional cases in connection with any of these maladies are deserving of careful record. The same may be said of retinitis due to acute nephritis of previously healthy kidneys; such cases are said to occur occasionally, especially after scarlet fever.

Eyre* records the case of a man, aged 50, with neuro-retinitis and the characteristic pattern of white dots around the yellow spot, malaise but no distinctive symptoms, and urine, for the first 10 to 14 days of the illness, free from albumin and casts. He died 2 months after the commencement of failure of sight (which was one of the earliest symptoms, and dated only 3 days before the first ophthalmoscopic examination), uræmic and

* Eyre, Ophthalmic Review, vol. xvi, p. 275, 1897.

dropsical, and at the post-mortem the kidneys were swollen and enlarged (together weighing 12·5 ozs.), the capsule non-adherent, cortex swollen and lighter in colour than the pyramids, which were extremely congested. The heart is not mentioned. No doubt in this case there was acute nephritis, but the fact that the casts found in the earlier period are specially stated to have been granular and hyaline, and that no blood was found in the urine till later, seem to indicate that some degree of chronic nephritis had been present before. The absence of any note on the heart, and of a microscopical examination of the kidneys, also lessen the value of this otherwise carefully recorded case.*

In regard to albuminuric retinitis from chronic nephritis due to conditions of bladder, ureter, or pelvis of the kidney, I can mention the following cases:—

(1) A boy (No. 62), aged 15, who had been operated upon for stone when 4½ years old. Dr. Sharkey sent him to me with severe retinitis in February, 1889; the boy was ill and his urine highly albuminous. He was said never to have had scarlet fever. Arteries thickened; accentuated second sound; urine abundant (usually about 60 to 75 ozs. in 24 hours), clear, acid, S.G. 1010, containing albumin in variable, but often large, quantity. Discharged in improved health after 2 months' treatment as in-patient under Dr. Harley.

(2) A man, æt. 49 (No. 78), who for many years had had some degree of cystitis, following Holt's operation for stricture of the urethra performed when he was 35.

(3) An old man (No. 80), whose renal symptoms and consequent retinitis appeared late in life, when he was 76, apparently in connection with enlarged prostate and cystitis.

2. But the chief exception to the rule that the retinal changes depend upon chronic nephritis is seen in the albuminuric retinitis of pregnancy. It appears to be well-established that a peculiar form of kidney disease occurs in

* Dr. C. R. A. Sutton mentions briefly two cases of retinitis during a first attack of acute nephritis, but does not furnish sufficient details. Guy's Hospital Reports, vol. lii (1895).

pregnancy, the special character of which is rapid degeneration of the epithelium, such as is found in some forms of acute blood-poisoning. Though this condition is not a true acute inflammation,* the kidney so affected may pass with unusual rapidity into a state of chronic nephritis and contraction.† Chronic nephritis of the ordinary forms may, of course, be present before the first pregnancy. In connection with our present subject, what we have to ask for particularly is that in every case of pregnancy retinitis, any evidence as to the state of the kidneys before the first pregnancy should be recorded; proof on the one hand that they were diseased, or evidence, based on careful examination, that they were sound. [Mr. Marcus Gunn informs me that in all the cases of albuminuric retinitis of pregnancy that he has seen in recent years, disease of the retinal arteries has been well-marked. This observation is important if the retinitis in any of Mr. Gunn's cases occurred in the first pregnancy.—E. N.] The propriety or otherwise of prematurely emptying the uterus may depend in part upon the conclusion as to the character of the kidney disease, whether old and progessive, or recent and perhaps recoverable.

It is generally held that the prognosis for life in the renal retinitis of pregnancy is better than in the ordinary cases, and my own experience agrees with this. This does not of itself prove that the renal disease of pregnancy is peculiar; it may merely show that pregnancy acts by causing an exacerbation of pre-existing kidney disease, from which exacerbation the patient recovers after removal of the special cause. But examination of the facts does, I think, support the hypothesis that in many cases the kidneys were healthy until they were attacked by the special pregnancy disease. Thus out of 22 cases of pregnancy retinitis, of which I have notes, I know of only five deaths, and only one of these

* Herman, Article: "Eclampsia," Allbutt's System, vol. vii. Groenouw, Graefe-Saemisch, Handbuch, 2nd edn., Kap. xxii, 1901.

† Dickinson, Article: "Diseases of the Kidney," Allbutt's System, vol. iv.

(No. 13) occurred within 2 years of the retinitis. (The four others died respectively $3\frac{1}{4}$, $4\frac{1}{4}$, 7, and 7 years after the retinitis.) Six other cases, of whose death I have no record, are known to have lived more than 2 years (one of them at least 5 years, one 9 years, having had pregnancies subsequent to the one that caused the retinitis; one $5\frac{1}{2}$ years, one 11 years, one 10 years, having had two pregnancies since the first which caused the retinitis; one 13 years, one 24 years). So that of the 22, nine (or two-fifths) are known to have lived 2 years or more after the retinitis, whilst of the four known to have died, only one, as stated above, succumbed in less than 2 years. On the other hand, of 42 non-pregnancy cases in which I know the duration of life after the retinitis, only nine or just over one-fifth lived more than 2 years; and no less than 25 died within 1 year. So it seems that if the pregnancy patients survive the ordinary maximum at all, say 2 years, they are likely to live for several years and sometimes for the full term of life. As a rule, the retinitis of pregnancy occurs only once, but occasionally the history points to a second more or less definite attack.

Again, in the majority of my own cases retinitis has not occurred until after several pregnancies, and in many there was a history of several attacks of pregnancy dropsy, the ages of these patients varying from 29 to 41. In 19 cases where the point is noted, the retinitis occurred during the fifth, or a subsequent pregnancy, in no less than 14, whilst in four of the 19 (Nos. 31, 52, 74, 79) it came with the first pregnancy.

Although in two of these four first-pregnancy cases (Nos. 31 and 79) further pregnancies are known to have occurred, no return of renal or eye symptoms took place, and the patients lived at least 10 years afterwards. These two women were very young (19 and 21 years respectively) at the date of the first pregnancy and of the retinitis, and though one of them (No. 79), now at the age of 31, presents the signs of granular kidney, it seems not improbable that the kidneys in both of them were healthy before the original

pregnancy. In other three cases (Nos. 72, 91, 96), where the retinitis, though not occurring in a first pregnancy, was followed by many years' (at least 11, 13 and 24) freedom from symptoms, it is reasonable to draw the same inference. These five cases (Nos. 31, 79, 72, 91, 96) were briefly as follows :—

Elizabeth B. (No. 31). Seen in July, 1881, æt. 28. In first confinement, 9 years ago, was "blind from dropsy" for 2 weeks. Number of pregnancies since then not stated, but after one of them had three fits, and during two of them dropsy, but less severely than the first time, and with no return of failure of V. Two years ago ulcer of L. cornea, leaving scar and preventing good ophthalmoscopic examination. R. V. 6/18, slightly improved by −1·5 cyl.; pigment spots all over fundus, including y.s.; at y.s. also many round dull whitish dots in or beneath retina; o.d. pale; the pigment spots often rather angular; no atrophy of choroid.

Alice T. (No. 79). Dropsy began about 5th month of first pregnancy when æt. 21. At 6th month (May, 1893) convulsions and general dropsy; labour artificially induced; was unconscious 10 days, and as soon as consciousness returned was quite blind; a few days later Dr. A. B. Batley found o.ds. indistinct, and large hæmorrhages into retinæ; u. contained casts and much albumen. Dropsy quickly disappeared, health improved, and on June 18th, 2 weeks after total blindness was discovered, could see dimly with L., but R. still blind. In October, seen at Moorfields, R. V. fingers 1·5 m., L. barely hand reflex; general retinal haze, some characteristic bright white deposits, much disturbance of pigment epithelium, and some blotches of increased pigment; o.ds. not much altered. U. hyaline casts and considerable albumen. About November V. rapidly improved, and she was able to resume her work in a drapery shop. Three years after first pregnancy Dr. Batley again induced artificial labour for commencing dropsy and albuminuria at 7th month of second pregnancy. Sight not affected. Two years after that, third confinement at full time (æt. 26) without recurrence of symptoms; child did well. May, 1903, now æt. 31, widow 3 years. V. has been as now since

about November, 1893. R. – 3 D. cyl. 6/9 partly, L – 2 D. cyl. with – 1 D. sph. 6/12; much disturbance of epithelial pigment about y.s., and some spots of increased pigment; no white deposits; o.ds. normal colour; arteries not bright, but one in L. eye compresses its companion vein decidedly. Radial arteries, especially L., thick and difficult to compress. Heart, second sound much accentuated, and probably both ventricles hypertrophied (Mr. L. J. Paton); u. 1030, high colour, acid, cloud of albumin to heat, nitric acid and picric acid. Considers herself well, and lives carefully.

Mrs. H. (No. 72). Two pregnancies, with interval of several years; second ended at 8th month, æt. 39, child living, albumin and failure of V. shortly before confinement. 5 to 6 months after failure of V. seen with Dr. A. C. Turner; subsiding characteristic neuro-retinitis of both; V.R. 6/24, L. 6/12. April, 1903, æt. 49, Dr. Turner writes that there have been no more pregnancies and she keeps fairly well, but that V. became slowly worse after I saw her and she is now quite blind of both eyes.

Mrs. R. (No. 91). Seen in 1896 and again in 1899, when æt. 65. Six pregnancies between ages of 29 and 41, and had albuminuria during several of them; all either still-born or miscarriages. About 8th month of No. 6 V. failed in both eyes "from albuminuria;" artificial labour induced; V. improved but not to full recovery. Still has albumin at times and has to diet carefully. V. and ophthalmoscopic changes the same at both her visits to me (1896, when æt. 61, and 1899 when 64); R. 6/18, L, 6/60; changes symmetrical, but more in L.; o.ds. pale, retinal vessels not obviously changed, patches of epithelial denudation, with some increase of pigment, at central region, y.s. invaded in L., but free in R.

Mrs. A. (No. 96), when æt. 36, late in a pregnancy, V. failed in both eyes, continued bad till confinement 6 weeks later, and got much worse a few days after birth of child. About 2 weeks after confinement V. began to improve, but never became good again; when at worst was nearly blind. No note as to albumin at that time; but husband (a doctor) says it is now normal. Seen by me for some recent further failure of V., January, 1897,

æt. 49; V. 6/60 with each, and with H. As. 4 D. corrected just reads up to 3 J.; many old pigment spots and pale spots about y.s., and at periphery, both eyes: in R. some fresh hæmorrhages and a single white patch; o.ds. dirty darkish colour and somewhat hazy; retinal arteries small and very bright.

Whilst on this subject of pregnancy retinitis, certain cases may be mentioned in which the sight fails soon *after* confinement, remains very bad for several weeks, and then returns more or less. We do not know the condition of the fundus during the active period in these cases. When seen some time after recovery, traces of past optic neuritis are found in some of them, but in others no visible change remains, and I have never seen signs of widely spread retinitis.* None of the cases that I have seen gave any history pointing to eclampsia, but on the other hand they are not explained either by flooding, or obvious kidney disease. I think that these cases deserve attention, as perhaps furnishing a link between neuro-retinitis from loss of blood, which, after all, may in a sense be toxic, optic neuritis in puerperal polyneuritis,† uræmic blindness, and the more acute examples of albuminuric retinitis.

I saw an additional and well-marked case of this kind with Mr. Doyne, at Oxford, only a couple of days ago. A woman, æt. 30, lost her sight absolutely a fortnight after her first confinement in June, 1902. Optic neuritis was diagnosed by an ophthalmic surgeon in Manchester. The urine was reported, she says, to be natural. She had no fits, and though the labour was instrumental (at the 8th month), she made a good recovery except for weakness. The blindness came on almost immediately after she got up from bed; she was suckling the baby, and did so till it died at 10 weeks of age. After some weeks she began to see light, and improved a little throughout the winter; latterly the improvement has been more marked, and she can now (July, 1903) read short words of print equal to about six Jaeger, and sees about

* Nettleship, R.L.O.H. Reports, vol. xiii, p. 97 (1891).

† Turney, St. Thomas' Hospital Reports, vol. xxv, 1897. "Polyneuritis in Relation to Gestation and the Puerperium."

4/60. The discs are very white, with some haze along the vessels, the arteries are not bright and there are no signs of past retinitis. The urine, tested on 28th August by Dr. R. M. Wood, is free from albumin, and though the second sound is somewhat accentuated, Dr. Wood finds no proof of cardio-vascular changes.

3. Influence of age and sex in renal retinitis (still omitting pregnancy cases).

Sex. In my own cases (numbering between 80 and 90) I find a large excess of males, viz.:—56 males and 30 females, or 64 per cent. and 36 per cent. Miles Miley, in 51 cases found 38 males and 13 females, or 75 per cent. and 25 per cent.; Schlesinger* in 43 cases, 29 males and 14 females, or 68 per cent. and 32 per cent. These figures, 123 males and 57 females, in all 180 cases, show 68 per cent. males and 32 per cent. females.† These proportions, about 2 males to 1 female, are almost the same as in chronic kidney disease (Dickinson and West),‡ and this is what we should expect.

Age. The age of patients of both sexes, with ordinary albuminuric retinitis, ranges between 30 and 60 in about two-thirds of the cases (54 out of 85 in my series), the most prolific single decade being from 50 to 59 (22 cases out of 85).§

If we include the pregnancy cases, the three decades (30 to 60) show nearly equal numbers, and yield together nearly 75 per cent. of the total (69 out of 107); the most prolific decade for the pregnancy cases being between 30 and 39 (10 out of 22 cases). This fact accords with the statement already made, that usually several pregnancies are required to produce such a renal state as will cause retinitis, but it proves nothing as to the condition of the kidneys prior to the first pregnancy.

* Schlesinger, Graefe-Saemisch, new edition, lief. 26-27, p. 97.

† C. S. Bull, however, found only 55 per cent. males and as much as 45 per cent. females.

‡ Dickinson, Clifford Allbutt's System, vol. iv. Samuel West, Lettsomian Lectures, "On Granular Kidney and Physiological Albuminuria," 1900.

§ Eales found the largest proportion of cases in the decade 55–65.—Birmingham Medical Review, 1880.

It is interesting to observe that so far as my small numbers show, the prospect of life seems to be better when renal retinitis comes on after 55 than before; for of my 10 patients who are known to have lived more than 2 years, no less than 7 were above that age when the retinitis occurred, viz.:—56, 57, 60, 64, 65, 75, 76 years respectively. Curiously enough the other 3 patients, who lived an unusually long time after the retinitis, were very young when it came on viz.:—5½, 21, and 23 years of age respectively.

The relative sex frequency is much the same after the age of 60 as before, 10 patients aged 60 and upwards being male, and 5 female, out of 15.

We are in need of more information as to cases of juvenile renal retinitis. I have seen 10 cases in patients under the age of 21 (Nos. 17, 19, 21, 44, 49, 55, 62, 98, 108, 109), and have found 14 others published in sufficient detail. Of these 24 patients, 10 were males and 14 females, almost the reverse of the rule. Of my own 10 cases, 1 (a boy) had been operated on for stone, 1 (a lad of 20 years) suffered from hereditary syphilitic keratitis, and 3 (a boy of 16 and 2 girls of 19 and 12 years) gave a history of scarlet fever about 9 years previously; in the remainder both scarlet and rheumatic fever were denied. I know the result in 6 of my 10 cases:—4 died within 5 months of the retinitis; one (No. 109) lived for 3½ years, dying of phthisis with amyloid disease of many organs; and one (No. 49) is known to be living and apparently well at the age of 25, nearly 20 years after her eye disease. In regard to the nature and cause of chronic kidney disease in children, it is interesting to note (1) Professor Rose Bradford's statement that the atrophic form of chronic Bright's disease, with small white or mottled kidneys, usually occurs in young subjects and is probably not directly related to granular kidney ("The Lancet," 1903, Vol. II, p. 3); [(2) Dr. George Carpenter's opinion, expressed in the discussion on my paper that evidence is accumulating in favour of chronic renal disease in children being often due to hereditary syphilis; (3) Mr. Hartridge, in

the same discussion, mentioned a case of renal retinitis, now under his notice, in a boy, aged 12 years, who is probably the subject of hereditary syphilis.] The 6 cases above referred to are as follows:—

Mary S. (No. 17). Good health till æt. 18, when she had an illness called "inflammation of bowels," and catamenia ceased for a year. Four months before admission into St. Thomas's Hospital another attack of pain in belly with severe constipation; got well from this, but 2 months ago V. failed and has got worse. On admission, 13th February, 1879, æt. 20, single, ill-grown. Has only p.l. Very severe retinitis of hæmorrhagic type with no white patches, but some patches of more or less complete *choroidal* atrophy, probably due to previous hæmorrhages from choroidal vessels. Died 2 months later, some absorption of retinal hæmorrhages having taken place. U. slightly albuminous at some trials, quite free at others. *Post-mortem.*—Kidneys granular, extremely contracted, tough and pale, cortex much wasted; L. ventricle much hypertrophied (an inch thick); pericardium n.; old R. pleurisy. Pregnancy not explicitly negatived.

Louisa D. (No. 19). Measles and whooping cough in infancy; never scarlet or rheumatic fever. Sight defective for 6 weeks before admission, and 17 days before admission a fit with loss of consciousness for several hours. Admitted at St. Thomas's Hospital, 4th June, 1879, æt. 14, under care of Dr. Stone. R. hemiplegia and paralysis of R. external rectus; systolic bruit; u. considerable albumin, a few blood-cells, no casts. Catamenia began 6 to 8 months ago, but have stopped for last 3 months. Severe characteristic neuro-retinitis with much swelling, and the radiating pattern of white deposits around y.s. 30th, V. much worse; urine contains more blood. August—another fit; extensive detachment of retina in each eye. September 23rd.—Died after convulsions. *Post-mortem.*—Heart, great hypertrophy of L. ventricle; old double pleurisy; kidneys, R. reduced to 1 oz. weight, L. 5 oz., granular, capsule adherent and leaving granular surface; brain, large old hæmorrhage just outside L. lateral ventricle. (This case was published by my then house surgeon, Mr. Davidson, in Trans. Ophth. Soc. I. p. 57., but I have

now added some other facts from my own notes made at St. Thomas's Hospital.)

B. (girl, æt. 11), under Dr. Bristowe's care at St. Thomas's Hospital, 11th July to 5th November, 1879, when she died. There was no *post-mortem.* Admitted for headaches and vomiting. Never had scarlet fever. 17th July I found double neuro-retinitis, suggestive of renal disease. U. 1012, a trace of albumin. By end of August I noted "receding renal retinitis; is now quite blind." 5th November—Died.

Thomas H. B. (No. 108). Healthy at birth; had rickets and at æt. 16 months stopped growing, head enlarged, and he began to pass large quantity of u.; æt. 4 years intelligence began to fail. Scarlet fever æt. about 7. Admitted 6th March, 1880 (Dr. Sharkey and Dr. Bristowe; my ophthalmic notes). Tibiæ bent from old rickets; u. 1010, much albumin, a few blood-cells, no casts, quantity about n.; o.ds. hazy; œdema of feet and hands. 11th.—Decided diffuse neuro-retinitis with grey swelling of retinæ. 17th.—Died. *Post-mortem.*—Heart somewhat dilated on both sides; aortic valves diseased. R. kidney 4½ ozs., small, cystic, no visible healthy structure, capsule adherent; L. kidney absent; no trace of it, its vessels or ureter. Dura-mater thick and adherent to skull, parietal bones thick and heavy, brain looks natural.

Theresa R. (No. 109). August, 1876, came to me at the South London Ophthalmic Hospital. She was æt. 12, but undergrown, and looked only 9, and she had enlarged submaxillary glands; severe neuro-retinitis, with many hæmorrhages in retina and some perhaps in choroid; no typical white patches; opacities L. vitreous. U. cloud of albumin repeatedly found. Some hypertrophy of L. ventricle (Dr. Barlow). First-born of 7, of whom 4 were living. Had "inflammation of lungs" æt. 13 months and mild scarlet fever æt. 4, and soon after that a vague illness in which became very weak for a time. In September, 1876, irido-cyclitis of L., with vascular deposits in angle, began and slowly progressed to blindness and shrinking, and in October, 1879, I excised the eye and found detachment of retina. R. had meanwhile recovered from 20/0 to 20/40 with pale o.d., small arteries and some spots like choroiditis. From 4th February, 1880, she was under Dr.

Harley's care, at St. Thomas's Hospital, till her death on 8th April of that year, at the age of about 15½, with advanced phthisis, albumin having continued in the urine till the end. *Post-mortem.*—Dr. Sharkey found old pericarditis and some hypertrophy of both ventricles; kidneys granular with adherent capsule, R. only 1½ oz., L. 5¼ ozs.; lungs destroyed by very large cavities lined by suppurating membrane, but no tubercle found in them. Intestines showed tubercle and some ulceration of Peyer's patches. Liver much enlarged, smooth; spleen enlarged and "sago-grain." Well-marked amyloid reaction with iodine in liver, spleen, L. kidney, and small intestines.

Beatrice H. (No. 49) had whooping cough and measles in early childhood; no scarlet or rheumatic fever; no diphtheria. Is first-born of four. Father has gout in ankle. When æt. 5½, ill with pains in loins and failure of V.; the late Mr. Haynes Walton saw her for the sight, and is reported to have said she had "Bright's disease;" no fits, but was very ill. V. did not begin to return for 4 months. At Moorfields, December, 1886, æt. 8; very timid: stunted and undergrown, patchy congestion of cheeks, heart's impulse increased and apex in nipple-line, radial artery too hard; u. 1010, cloud of albumin (repeated examinations by Dr. Herringham)—V. fairly good, but not normal. O.ds. very white, arteries shrunken, veins show thick white lines; pigment disturbance and some shining white spots at y.s. Seen again in 1887 (March and August), and 1889 (October), and urine each time of low S.G., and contained a little albumin. For a time continued to have much frontal headache, but in other respects improved and grew bigger and stronger. V. was always 6/36 with each eye. In November, 1891, æt. 13, much stronger and better grown; V. of R. 6/36, L. 6/24; U. 1010, but no albumin (single examination). In June, 1903, Dr. W. J. Drew, of Egham, where the girl formerly lived, kindly wrote that he had enquired and heard that she was grown up and in good health. She must now be 25.

4. We recognise two principal factors in the production of albuminuric or, more correctly, renal retinitis, a morbid state of the blood, and a diseased condition of the walls of the

retinal arteries,* and in most cases we have to reckon with both. The blood-state is the chief cause in the severe acute cases with great œdema and effusion, some of which, *e.g.*, the favourable pregnancy cases, recover both health and sight. Arterial disease takes the more important share in many of the less violent cases. Then, we meet with arterial disease, hæmorrhages and retinitis, and white patches, without albumin; and finally cases of arterial disease only—hyaline thickening of coats, with or without exaggeration of the light streak—occasionally with albumin, but more often without.

I do not propose to dwell on the blood-state in renal retinitis. But there is plenty of room for careful clinical work in regard to the diagnostic significance of visible changes in the coats of the retinal arteries.

When we see the retinal arteries thickened and hyaline looking, whether they have caused venous hæmorrhage by compression or not, are we justified in inferring the presence of chronic nephritis if the urine (examined repeatedly) is free from albumin, not of very low specific gravity, and the heart not demonstrably hypertrophied? Dr. Samuel West† believes the diagnosis of granular kidney is justified when we find high pulse-tension, with thickened artery and retinitis, even without albuminuria, and he appears to think that the pulse-tension and thickened artery alone are enough in some cases without either retinitis or albuminuria. The ophthalmic observer may, therefore, fairly suspect an early stage of granular kidney disease whenever he diagnoses decided hyaline thickening of the retinal arteries. The suspicion will be much strengthened if the patient be comparatively young. It is well, therefore, to look for the appearance of such arterial disease by routine in *young* subjects.

This hyaline-fibroid thickening of the retinal arteries is now well-known to be indicated by intensification of the bright streak and compression of the veins where they are

* Gowers, 1876; Brailey and Edmunds, 1881; Marcus Gunn, 1892 and 1898; Hertel, Heidelberg Congress, 1900.

† Samuel West, *loc. cit.*, p. 37.

crossed by arteries. The condition, though probably seldom confined to the arteries of the retina, is, doubtless, often spread unequally throughout the system; indeed, in regard to the retina alone the appearances may be conspicuous in one eye, and insignificant or even absent in the other, whilst even in the same eye they are by no means always equally distributed along the affected vessel or vessels.

I have not myself had the opportunity of tracing a case in which uncomplicated disease of retinal arteries was proved to be followed after some years by the signs of chronic nephritis. Mr. Marcus Gunn,* has however, recorded a very important instance in which a woman, at the age of 51, had bright retinal arteries, and a little hæmorrhage into the vitreous of one eye, but no albumin and no renal symptoms; when 56, there were retinal hæmorrhages and albumin was sometimes present; from 58 to 59 more retinal hæmorrhage, retinal patches, a cerebral seizure, and albumin more frequent; at 61 retinitis worse, cerebral degeneration, uræmic symptoms. I anticipate that other cases of this kind followed from beginning to end will be forthcoming.

[Mr. Marcus Gunn kindly allows me to add the following unpublished cases and remarks, showing, as he believes, that marked arterial disease with albuminuria may sometimes come on comparatively quickly. (1) The patient, a man who had been seen several times during about 10 years by Mr. Gunn, quickly developed serious bad health with albuminuria, degeneration of retinal arteries and hæmorrhages, after a very bad attack of influenza; he died 18 months later of intracranial hæmorrhage. (2) In another patient, whose health suffered greatly after severe influenza, albuminuria, degenerated retinal arteries, and retinal hæmorrhages were found.

Mr. Gunn suggests a comparison between such post-influenzal cases and the albuminuric cases of pregnancy, the arterial and renal disease in both being, he supposes, due to a comparatively rapid poisoning, but the process being usually less severe when caused by pregnancy than by influenza.]

* Gunn, Trans. Ophth. Soc., vol. xviii, p. 356, 1898. (Case 10.)

Whether the thickening of retinal arteries specially described by Gunn and others, is so useful a diagnostic sign of granular kidney when seen in elderly persons, is, I think, an open question. For instance, in my own notes on this point, either the silver-wire appearance, or marked compression of veins by arteries, in patients over 40, has been recorded much more often in women than men. My cases (35 in number), were, however, all in private practice, and may contain some source of error, such as the greater total number of female than of male patients. Mr. Marcus Gunn tells me that he believe she also has seen more women than men with degenerated retinal arteries. In his published series of cases* from the Queen Square Hospital, however omitting such as had albuminuric retinitis, there were 12 males to 9 females, which is more like the normal proportion in chronic renal disease. But even if hyaline thickening of the retinal arteries after middle age should prove to be a less valuable sign of incipient chronic nephritis than it probably is in younger subjects, we must still take it as a sign of the danger of cerebral hæmorrhage.†

5. The general opinion is that the particular characters of the retinitis do not afford any guide to the kind of chronic kidney disease present in a given patient. Dr. Samuel West, however, maintains that the so-called "exudative," or "inflammatory" form of retinitis, *i.e.*, retinitis with much œdema and general haze, indicates parenchymatous nephritis, whilst the "degenerative" variety, *e.g.*, a case characterised

* Gunn, *loc. cit.*

† E. Hertel (*loc. cit.*), who has examined the retinal vessels in a series of patients with widely spread angio-sclerosis, divides the microscopical changes in the arteries and veins of the retina into two groups, those associated with age (senile changes) and those due to inflammation. In the former all the layers show an increase of elastic tissue, and the lumen of the vessel is enlarged, these changes affecting the whole course of the vessels. In the latter the alteration, often limited to certain parts of a vessel, appears in the form of localised thickenings of the intima, which may cause narrowing of the lumen, and are, as in the senile form, also composed of newly-formed elastic tissue.

by the presence of the well-known figure of bright white dots or patches around the yellow-spot, with little or no general haze, but often with decided thickening of the retinal arteries, points to granular kidney. I agree with Dr. West, that the more violent cases of retinitis are chiefly toxic, and the milder, more chronic ones, often chiefly vascular in origin. But I think it is unnatural to draw sharp distinctions between the "exudative" or "inflammatory" and the "degenerative" varieties, or to associate either form with any particular kind of chronic nephritis. If we watch cases from an early stage to the end, we shall find that both in interstitial and in chronic parnechymatous nephritis, the retinitis may be either intense or comparatively mild.

No. 19, already quoted (p. 329), is an example of very severe retinitis, with all the changes in advanced granular kidney disease. In No. 18, a man, æt. 31, had, when I saw him on 3rd October, 1879, diffuse haze and œdema of o.ds. and retinæ without either hæmorrhages or white patches of any kind. A month later (November 5th) o.d. and retinæ clearing, bright white dots at y.s. in R., none in L. Three weeks after this (November 26th), retinæ nearly clear of diffuse haze, radiating bright dots at y.s. very striking; some pigment spots now visible; some hæmorrhages now present. He lived till March, 1880; the kidneys weighed $14\frac{1}{2}$ ozs., capsule non-adherent, surface smooth and generally pale. Heart much hypertrophied.

If the eyes in No. 18 had been examined for the first time in November, the retinitis would, I suppose, have been called "degenerative," and it seems never to have been decidedly "exudative," yet he had "large white" kidneys.

To my mind it is clear that there is only one sort of renal retinitis, and that, apart from arterial disease, the many varieties of change seen during life indicate only different stages and degrees of (*a*) general œdema,* (*b*) exuda-

* Distension of the peri-vascular lymph-spaces of the retina is, in addition to general œdema, described by Weeks, Arch. of Ophthalmology, vol. xvii, p. 276, 1888.

tions into the nerve-fibre layer (Plate, Figs. 1 and 2), and (*c*) spots or patches of opacity in the deeper layers due to degeneration of fibrinous or albuminous effusion in the inter-granule layer (Figs. 3 and 4), and perhaps to changes in Müller's fibres. The optic neuritis and retinal hæmorrhages so often present in varying degrees are not characteristic, though they increase the difficulty of interpreting the morbid appearances. The exudations (*b*) into the nerve-fibre layer form white or greyish-white patches of moderate size, *i.e.*, large enough as a rule to be easily seen by the indirect method; they have no constant shape or mode of grouping, but are scattered usually around the O.D. region; they commonly show an ill-defined, or "woolly," or soft-edged outline, which merges rather gradually into the clear or comparatively clear retina around, and not infrequently they lie in front of the retinal vessels. These patches form early in the case; they may be present a week or two after the patient begins to notice failure of vision, and perhaps even earlier. They are often, but by no means always, accompanied by general haze and marked œdema of the retina. The individual patches often disappear in a few weeks, but fresh ones often form later, so that patches of this kind are apt to be found both early and late in the case. The other kind of opacity (*c*) appears ophthalmoscopically in the form of intensely white sharply-defined round dots, which, when they become confluent, form spots or patches. They are variously described by authors as "chalky" or "glistening" white, or "yellowish-white," or "like fish-scales." These deposits are specially apt to occur around the yellow spot, and when in that situation, they are so arranged as to form the well-known stellate or radiating figure. They lie deeper than the soft-edged patches (*b*), and never in front of the retinal vessels. They are not present in the earliest period of the retinitis, but may be expected to appear, say, from 4 to 8 weeks, or later, after the onset, as in Case 18 above quoted and in others that I could mention.

Fig. 1.

Fig. 2.

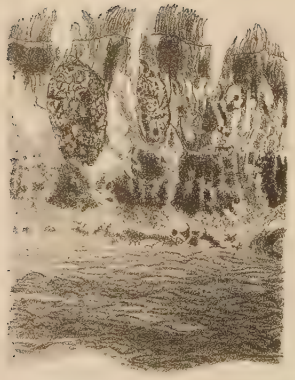

Fig. 4.

Fig. 3.

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To face p. 336.

Description of Plate.

Illustrating Mr. Nettleship's Paper on Renal Retinitis.

Fig. 1. Shows a large swelling in the nerve-fibre layer of the retina close to the optic disc. There are also amorphous (fibrinous) deposits (*a*) and patches of partly disintegrated blood-corpuscles (*b*) in the inter-granule layer. The letters O D are in the situation of the physiological pit.

Fig. 2.—A smaller swelling in the nerve-fibre layer.

Fig. 3.—Fibrinous deposits in the inter-granule and outer-granule layers.

Fig. 4.—Similar deposits more highly magnified.

The above figures are from sections of the retina of a man æt. 43 (No. 25), in whom Dr. Sharkey found albuminuric retinitis in February, 1880, and who died 3 months later. A few days before death I examined the eyes again and found abundant changes still present. They show that, as stated on pages 336 and 337, in albuminuric retinitis of long standing, the soft-edged patches in the nerve-fibre layer and the sharply-defined deposits in the deeper layers may be present at the same time.

(Figs. 1 and 2 from drawings by the author. Figs. 3 and 4 from micro-photographs by Mr. J. Herbert Parsons.)

Thus in No. 30, a man, æt. 29, had in July retinitis with slight œdema and haze, many soft-edged or woolly white patches, but no bright dots, though these were very carefully sought for. In August (1 month) woolly patches less numerous, but general haze increased, and characteristic bright white dots now present at each y.s. In October (4 months) retinæ had cleared, o.ds. greyish and nearly clear, bright dots still present at y.s. He had on admission signs of parenchymatous nephritis, general dropsy, scanty urine with much albumin and granular and hyaline casts, dyspnœa and some cardiac hypertrophy; he was much better after 6 months' treatment.

The greater the early haze and œdema, the larger is the amount of these intensely white, late, degeneration deposits.* When they appear, the earlier soft-edged patches have often to a large extent cleared off; they last much longer than the soft-edged patches, but if the patient lives they certainly lessen (Cases 44 and 30), and probably disappear in the course of many months, though not in a shorter time. In severe and prolonged cases the different forms of opacity are often so abundant, and so mingled with hæmorrhages and general haziness and discolouration of the retina, that no analysis is possible, and I think that many of the discrepancies noticeable in the published descriptions of renal retinitis have arisen from choosing for illustration cases of great severity and long standing, or cases in which the duration of the changes was not recorded.

6. It is well known that various other constitutional or local conditions produce retinitis or neuro-retinitis resembling, and sometimes indistinguishable from, that caused by disease of the kidneys. The only variety that I think we need dwell upon, however, is the retinitis associated with glycosuria. Retinitis in patients with diabetes is fairly

* The extreme brilliancy of these spots, as seen in ophthalmoscopic examination, suggests that they are of fatty composition; but microscopical examination shows them to be either amorphous or composed of a fine fibrinous network. I have found that neither ether nor chloroform affects their appearance in sections.

common, and, in my experience, is much more frequent in private than in hospital practice.* Thus, of my 59 cases, only seven were in hospital patients. In many the urine contains a little albumin as well as sugar, and in these it may be that we are sometimes dealing with ordinary albuminuric retinitis due to the nephritis that occurs late in diabetes. But I have seen at least a dozen in which there was no albumin, and cases have been published in this country by Stephen Mackenzie,† by the late James Anderson,‡ by Juler§ and by Rockliffe,‖ and in Germany by Hirschberg.¶ I have also recorded cases.** There can, therefore, be no doubt that retinitis may be caused by diabetes. Diabetic retinitis has a strong family likeness to renal retinitis, but differs from it in the absence of the soft-edged or woolly patches, and of the stellate or radial arrangement of the white deposits around the yellow spot, and there is usually no œdema. The hæmorrhages so often present in diabetic retinitis are more often round and deeply seated than linear and superficial, as in renal retinitis; in diabetes they are often derived from capillary aneurysms, not from the rupture of larger vessels in the nerve-fibre layer. The white deposits take the form of irregular masses or clumps rather than dots or round patches, and are often arranged in a rude zone or ring at the circumference of the macular area. In a few instances hæmorrhages into retina and vitreous form the chief feature, and these are, as would be expected, not characteristic of diabetes.

I have the impression that the life prospect in the retinitis of diabetes is better than in ordinary renal retinitis, but my data are too small to justify a positive statement. However,

* Hirschberg makes a similar statement. Centralblatt, 1886, p. 193.

† Mackenzie, R. L. O. H. Reports, vol. ix, 1877.

‡ Anderson, Ophth. Review, vol. viii, 1889.

§ Juler, Trans. Ophth. Soc., vol. xii, 1892.

‖ Rockliffe, *ibid.*, vol. xiv, 1894.

¶ Hirschberg, Centralblatt, 1891, pp. 18, 68.

** Nettleship, Trans. Ophth. Soc., vol. ii (1882), and vol. 6 (1886), with ophthalmoscopic drawing.

this may be, there is no doubt that the age of the patients is generally greater in the diabetic cases. Of 82 patients with retinitis in diabetes (59 of my own and 23 published), only 1 was as young as 35, and the great majority (66) were between 50 and 70. Whilst of 107 with albuminuric retinitis 29 were 35 or less; 46 between 36 and 49; only 32 between 50 and 70 or upwards. Of the diabetic cases 65 per cent. were men, 35 per cent. women, about the same proportion as for the renal cases, and not very different from the respective deaths of male and female diabetics of all ages, which, according to Saundby,* are about 57 males to 43 females.

I have already mentioned that in renal retinitis the prospect for life seems to be better in old persons than in those below 50. If the life prospect in diabetic retinitis is better than in the average renal cases, this may be because the diabetic patients are usually older when the retinitis comes on.

7. Many other points upon which further clinical or pathological information is desirable might be mentioned. I find very little in my notes about either scarlet fever or inherited syphilis as causes of the chronic renal disease leading to retinitis; I hope others who have made more careful enquiries can tell us something.

The typical retinitis of renal disease is of course nearly always symmetrical, though sometimes very unequally so. I have seen several cases of chronic renal disease with changes confined to one eye; in most of these the retinal disease consisted chiefly or entirely of hæmorrhage, the arteries being much diseased. But in one fairly typical case of retinitis (No. 76), the second eye was not attacked till several months after the first.

In another case (No. 59), a man of 48 had rheumatic fever (5 weeks in bed), and 5 months later lost the sight of his L. eye instantaneously from embolism or thrombosis of the retinal artery; soon after this he had an attack of temporary aphasia,

* Saundby, Allbutt's System, III, p. 198.

and then L. hemiplegia, and he was now told that his urine contained albumin; then the R. eye failed with typical albuminuric retinitis, but the L. (embolised eye) in which the arteries were extremely reduced, the disc pale, and V. only 20 J., showed no recent changes at all.

From this case we may probably infer that a retina atrophied by previous disease is unable to take on the œdema and other changes of renal retinitis. Case 64, given below (p. 341), probably illustrates the same point. In another case (No. 22) the patient's L. eye was highly myopic, and showed only two small hæmorrhages and a little mottling of doubtful significance at the yellow-spot; the R., with nearly normal refraction, had typical well marked retinitis.

Knies* mentions having seen "pure hæmorrhagic retinitis" in the hitherto healthy eye of an albuminuric patient, whose other eye had been blinded a year before by retro-bulbar neuritis; the retinitis spared the blind eye.

[Dr. Reeve, of Toronto, related a case of albuminuric retinitis in a patient with myopia 18 D., stating particularly that the retinal changes due to the albuminuria were comparatively slight, though the myopic changes in the choroid were pronounced.]

In this connection it would be interesting to know of instances in which renal retinitis has recurred in the same eye after the first attack had cleared off. I have notes of several cases in which it is almost certain from the history that more than one distinct attack did take place, but I have never actually seen two successive attacks. The following appear to be examples:—

No. 9, a man of 28. His sight failed in June, 1877, when in hospital for kidney disease under the care of Dr. George Johnson and Mr. Soelberg Wells. V. improved and he believes got perfect, but 6 months later (December), renal symptoms returned and sight became worse. In January, 1878, I found (*a*) severe albuminuric retinitis with much swelling, and with detachment of the

* Knies, The Eye in General Diseases, p. 306 (American Translation, 1895).

lower part of each retina; (*b*) many very black pigment spots, some of which, especially at the periphery, were in front of retinal vessels, and also some sharply defined areas "like brown paint," on which the normal epithelial pigmentation appeared to be intensified without being disturbed. The changes under (*b*) were probably left by an attack of retinitis in June, 1877.

In Case 29 the patient, male, 49, had typical retinitis in both eyes when I saw him in May, 1881, and, in addition, at the periphery of L. fundus only, spots of pigment surrounded by a pale zone and evidently old. This eye had been dim for a time in the previous autumn and had recovered, the R. not being noticeably affected at that time.

In Case 64, a woman had dropsy without failure of V. during her third and fourth pregnancies. In the 7th pregnancy dropsy again, and this time V. failed at about 4th month; artificial labour at 7th month. When æt. 29, 5 months after onset of bad sight, Mr. Lawford, in May, 1889, found R. 6/60, L. 6/18, with pale hazy discs, small arteries, bright dots at Y.S. region and pigment spots at equator. Became pregnant again about August, and was confined at full time (8th child) in April, 1890; she said that sight had "failed again" during this pregnancy, and that shortly before confinement she became totally blind. I saw her the following July, æt. 29, quite blind; all the white dots had gone, and only some epithelial changes remained at the Y.S., with the O.Ds. extremely white, and the pigment dots as noted by Mr. Lawford. The appearance suggested additional degeneration of the optic nerves rather than a recurrence of retinitis.

Case No. 50 was that of a woman pregnant 7 times in 7 years. Dropsy during second pregnancy; failure of sight, lasting for 6 weeks each time, during the fifth pregnancy 2 years ago, the sixth 6 months ago, and the seventh 2 months ago. It was for the last attack that she sought advice. All the children premature or stillborn except the second. When seen for third failure of V., January, 1887, æt. 32, typical renal retinitis with V. 6/18. No proof of any old changes, though the history points strongly to previous attacks.

Whether or not a relapse of true retinitis can occur, as I believe it may when no high degree of atrophy follows

the first attack, we have proof that recurrences of retinal hæmorrhage do happen in eyes that have passed through albuminuric retinitis; this was seen in Nos. 6 and 96 for example (see below).

In examining cases of albuminuric retinitis, we often find spots of black pigmentation sometimes surrounded by a pale ring; they, no doubt, represent little heaps of retinal epithelial cells, increased by proliferation* and the subsequent contraction of inter-cellular effusion. These pigment spots are generally scattered irregularly, but sometimes are specially abundant towards the periphery, a puzzling fact, since as they are a consequence of the retinal œdema and exudation, we should expect them to be most marked where the retina is thickest and most vascular.

In a few cases actual pigmentation of the retina is observed, as in Case 9, given above, and in the following:—

In Case 83, a woman, aged between 50 and 60, seen in 1894, had, in addition to hæmorrhages and bright white deposits at the Y.S. region, large areas of pigmentation, exactly like retinitis pigmentosa, but confined to the lower part of the equator in each eye. Dr. Knox Shaw, who has seen her more recently, writes to me that the hæmorrhages have recurred during the last few years, and that the retinal arteries have now become extremely small. Though the pigmentation was characteristic when I first saw her in 1894, she did not admit that her sight was worse at night.

In another (No. 96) a presumably eclamptic retinitis occurred quite late in pregnancy, seems to have become worse for a few days after the confinement, and then rapidly improved, V. remaining serviceable. When I saw her 13 years afterwards there were many pigment spots and pale spots both at the Y.S. and periphery, with small, very bright arteries and dirty haze of O.Ds.; vitreous clear. The changes might have passed for old syphilitic choroido-retinitis, but the history was much more like albuminuric retinitis, and, moreover, there were some

* Nettleship, Transactions of Ophthalmological Society, vol. 19, p. 63, 1899.

fresh hæmorrhages in one eye, which were the cause of her coming for advice.

Albuminuric choroiditis is mentioned by many writers, chiefly on the authority of Magnus's monograph, published in 1873.* Magnus could only bring forward a single case, that of an anæmic boy of 15 with albuminuria, casts and mitral stenosis, in whose L. eye a large patch of exudation extended from the O.D. to the Y.S., situated entirely beneath the retinal vessels. Judging from the description and plate, this patch resembled the solitary choroidal exudations with which we are all familiar and which appear to be sometimes tubercular, sometimes gummatous. Neither tubercle nor hereditary syphilis are mentioned in Magnus's account. The exudation disappeared completely in 3 weeks, and no changes were present in the other eye; 3 months later (4 months from the first examination) the renal symptoms were worse, but no changes present in either eye. Magnus also counted as choroiditis the pigment spots which were figured by Liebreich,† and also some cases resembling retinitis pigmentosa, described by Galezowski as "choroiditis nephritica." Notwithstanding the statements of Carl‡ and Knies§ that inflammatory foci are not uncommonly found in the chorio-capillaris in renal cases, I think that such pigmentary ophthalmoscopic changes, as have been just mentioned, should be considered as secondary to the retinitis,‖ or if choroidal at all, as caused indirectly by slow atrophy of the choroid from hyaline-fibroid thickening of its arteries. That the vessels of the choroid are often extensively diseased is well

* Magnus, Die Albuminurie in ihre Ophthalmoskop: Erscheiningen, 1873, Fig. 8A.

† Liebreich, Atlas, Pl. XI, Figs. 1 and 2.

‡ Carl, Hertzog, describes obliterative changes in choroidal arteries and capillaries leading to secondary changes of the pigment epithelium; also definite thickenings of choroid from cellular infiltrations.

§ Knies, *loc. cit.*, pp. 302 and 306.

‖ Nettleship, Trans. Ophth. Soc., *loc. cit.*

known; Weeks has found extravasations of blood into the choroid: and I have also found them in sections from one of my own cases.

Very marked night blindness is noticed occasionally.

One such case (No. 14) was seen in an alcoholic woman, aged 42, with atrophic changes 8 months after severe renal neuro-retenitis; there was no pigmentation of retina, but the retinal arteries were shrunken and one of them ensheathed by white opacity (peri-arterial inflammation). Another case (No. 33) was in a soldier invalided from India for "Bright's disease" at the age of 33. Two years later, in the early summer of 1883, he became rapidly night-blind, and we found contracted fields, pale discs, small retinal arteries and slight haze, but no actual proof of previous gross retinitis; V. from 6/12 to 6/24 according to the illumination. Urine, S.G. 1005, with much albumin. He had been out of work and badly fed for 3 to 4 months when the night blindness came on. In a third case (No. 67), similar to the last, a cabman, æt. 57, who had been underfed and sleeping badly for several months, found his sight failing rapidly at night in the spring of 1890, and we found his sight much worse for Bjerrum's gray types than for black and white. The retinæ were slightly hazy, and showed many small hæmorrhages close to the arteries, but no white patches of either kind were present, and none appeared during the 3 months he was under notice. Urine, S.G. 1010, a considerable quantity of albumin; pulse tension high.

I suggest that in each of these three cases the night blindness was functional, due to exhaustion by bright light in a badly nourished person, whose retinæ were already weakened by arterial shrinking and some degree of previous retinitis.

Mention has been made of white peri-vascular thickening in one of the cases referred to at an earlier part of this paper. This appearance is peculiar; it is quite different from the ordinary opacity bordering the blood column of the vessels near the disc so commonly seen in post-papillitic atrophy, from concentric opaque thickening with contraction

of the lumen, and from the bright "silver wire" appearance described by Gunn. The vessel, which may be either artery or vein, has its blood column entirely hidden for a longer or shorter distance by what looks like a coating of white opacity laid on outside the vascular walls; this coating begins and ends abruptly, the blood column disappearing and re-appearing without obvious alteration of size; sometimes there are little holes or gaps in the white sheath.* A good illustration is given in Fig. 1, Plate XII, of Gowers' Manual and Atlas. I remember seeing the patient from whom that drawing was made, and I have made notes of a good many cases since. It is probably a similar condition that is depicted by Frost† in his Atlas. Mules‡ has also written on the condition and given a coloured illustration. The appearance is not seen until the retinitis has lasted some time. I do not know whether microscopical examinations have been made.

Occasionally new blood vessels form in the vitreous humour. This rare change is, however, not characteristic of kidney disease; indeed, I believe that most of the examples have been seen in cases of diabetic and syphilitic retinitis. I have notes of it in only one renal case (No. 69). Mr. Frost gives one from a woman, æt. 54, with slight albuminuria, but does not mention sugar.§

Iritis in renal disease has been seen in two cases by Knies,‖ but he gives no particulars. Slowly destructive irido-cyclitis occurred in one eye in my Case 109 recorded above, but the inflammation in this eye was probably like that in the intestine and lungs, tubercular and independent of the kidney disease.

* An extremely accurate description of the ophthalmoscopic appearances of this peri-arteritis was given by Hulke in 1865, in an albuminuric case (R.L.O.H. Reports, vol. v, p. 25).

† Frost, Atlas, Pl. XL, Fig. 90.

‡ Mules, Trans. Ophth. Soc., vol. ii, p. 47.

§ Frost, *loc. cit.*, Fig. 91.

‖ Knies, *loc. cit.*, p. 306.

EPITHELIAL PLAQUES OF THE CONJUNCTIVA.

W. T. Lister, F.R.C.S., and W. Ilbert Hancock, F.R.C.S.

We bring forward the following cases of epithelial tumours of the conjunctiva, because in our experience they are very rare, and we think that their classification, ætiology, and certain points in their diagnosis are deserving of careful attention, and also are in need of further elucidation.

Case I.

Martin A., age 24, attended at the R.L.O.H., Jan., 1903, complaining of a small lump on the L. eyeball beneath the upper lid. He had noticed it for at least 10 years, but could not say if it had been present longer. He thought that in the last few years it had slightly increased in size, and he complained that at times *flakes* were detached from its surface by the friction of the upper lid, which, acting as foreign bodies, caused considerable irritation. These flakes he had himself removed on more than one occasion from the lower fornix.

On examination, an elongated oval growth was found in the bulbar conjunctiva, 6 mm. long, 2 mm. wide, situated above the cornea, but separated from the limbus by about 2 mm. The growth was slightly raised, about $\frac{1}{2}$ mm.; it had a sharply defined edge, and was freely movable over the underlying sclerotic.

The surrounding conjunctival vessels were somewhat injected, but the growth itself was *avascular*. Its colour was pale yellow and its surface dull, strikingly different from the normal bright conjunctiva. With focal illumination the surface was seen to be marked by parallel furrows running transversely to the long axis of the growth, a few less distinct furrows were seen running at right angles, *i.e.*, longitudinally with the growth. The lids were normal, there was no history of traumatism, there was no night blindness, and in every other way the eye was normal.

The growth was removed with a portion of surrounding conjunctiva and microscopic sections were made.

Case II.

Mildred S., æt. 15, came to the R.L.O.H., April, 1902, complaining of a small growth on the R. eyeball. Her parents had first noticed it 3 months previously, and could not say if it had been present before that time.

The growth was nearly circular, about 2 mm. in diameter, situated near the limbus, upwards and slightly outwards, for the most part in the conjunctiva, but encroaching about ½ mm. on the cornea. The conjunctival portion was freely movable on the sclerotic. It was sharply defined, about ½ mm. in thickness, of a pale yellow colour, dull granular surface, but in this case no furrows were seen. The surrounding conjunctival vessels were slightly injected. The growth was removed under cocain, but the patient returned a year later with a recurrence exactly similar in position and character. It was removed a second time and microscopic sections were made.

The lids were normal, there was no history of traumatism, no night blindness, and the eye was normal in every other way.

On Microscopic Examination the specimens removed from these 2 cases are found to be so similar that they may be described together.

In each the growth consists of a greatly thickened epithelial layer, which at the margin abruptly passes into that of the normal conjunctiva. The surface cells are squamous and somewhat horny; beneath these are several layers of cells resembling the "stratum granulosum" of the skin, showing well-marked granules which stain deeply. The deeper layers show distinct prickle cells; while in the deepest layers the cells resemble those of the normal conjunctival epithelium.

In the specimen from Case I, in which furrows were seen clinically, some fairly distinct papillæ are clearly visible. In the specimen from Case II, where no furrows were seen, no signs of papillæ are visible.

The subjacent connective tissue shows a patchy infiltration with small round cells, and the vessels are dilated; but in no

part does the epithelium pass down into the underlying connective tissue.

Case III.

J. H., a signal fitter, æt. 51. Three weeks before his visit to the Central London Ophthalmic Hospital, in April, 1899, he had been struck in the R. eye with a piece of stone. He said that no portion of the stone remained in his eye.

He had a small, white, nearly circular, sharply circumscribed growth on the conjunctiva on the inner side of the R. cornea, 3 mm. in diameter, raised about 1 mm., separated 1 mm. from the limbus. The blood vessels round the growth were dilated. The mass was dead-white in colour, with a few minute pink spots on the surface. It was freely movable on the sclera beneath.

The growth was completely removed with a portion of the conjunctiva surrounding it, and microscopic sections were made.

No foreign body was found in the growth, and the eye was otherwise normal.

Microscopic examination of the sections shows the growth to consist of a mass of epithelial cells. In the centre this is six to seven times thicker than the normal conjunctival epithelial layer, while at the margins it gradually becomes thinner. In this case there is no abrupt margin to the growth. The superficial layer consists of squamous cells which are becoming horny, and from this layer one or two processes of horny cells pass from the surface into the mass of epithelium.

Running through the mass a few dilated blood vessels with extremely thin walls are to be seen, and the pink spots seen macroscopically were evidently due to these vessels where they appeared on the surface. There are no definite fibrous tissue processes passing into the epithelial mass; nor do any epithelial processes pass into the subjacent tissue.

At the base of the growth there is some infiltration of round cells.

Case IV.

A case very similar to the last came up at about the same time to the R.LO.H. We regret that we cannot find the notes of this case nor the microscopic sections, but the case is distinctly

remembered. An elderly patient came to the hosptial with a circumscribed raised tumour on the ocular conjunctiva on the inner side of the cornea, but a little distance from the limbus. It was dead-white in colour, it had no pink spots, as in Case III, and was freely movable on the underlying sclerotic. The microscopic sections showed the growth to be nothing but a mass of epithelial cells.

Comparing these four cases:—

Cases I and II were young people, while Cases III and IV were well over middle life.

In Case III there was a history of injury, and it was after this that the growth was noticed. We think the injury was very likely the cause of the growth, some irritation being set up which caused hypertrophy of the epithelium.

In Cases I and II there was no history of injury, and the growths had been present for 10 years and 3 months respectively.

As to the cause of the growths in Cases I and II we are uncertain. It is possible, though we do not think it likely, that they are congenital and of the nature of the so-called *dermoids*. But they differ from the latter, in that they have neither hairs nor glands, and only in Case I does the growth show any sign of papillæ.

As already mentioned, there were none of the recognised appearances of xerosis of the conjunctiva. The site of the growth was not that usual in xerosis, the mass had not a frothy appearance, the surface could not be scraped off, there was no night blindness, and the patients were in perfect health.

Hocquard has described two groups of cases in his paper entitled "Plaques épithéliales da la Cornée," published in "Archives d'Ophth.", 1881.

(i) Emulsion patches, which apparently are similar or closely allied to xerosis.

(ii) Hypertrophic epithelial patches, occurring on the corneæ of injured eyes subjected to continued irritation.

From his description the latter would correspond with the white thickened epithelial patches seen fairly commonly on staphylomatous corneæ.

We think that our cases are closely allied in microscopic structure to Hocquard's second group, but these were *corneal*, whereas ours are *conjunctival*.

Jessop, in the XVI vol. of "The Transactions of the Ophth. Soc.," describes a case of a small growth on the ocular conjunctiva in a boy, similar to our Cases I and II, except that his growth was red and ours were yellow, but this difference might be accounted for by greater vascularity in the underlying tissue. The late Professor Kanthack examined microscopic sections of it, and described it as consisting of extreme thickening of the surface epithelium of the conjunctiva and increase of the papillæ.

The chief interest of Cases III and IV is, we think, their clinical likeness to epithelioma of the conjunctiva. Case III was thought by one of us to be very possibly epithelioma, and Case IV was seen by several surgeons at the Royal London Ophthalmic Hospital, and also thought possibly to be of a similar nature.

The correct diagnosis was made clear by the microscopic sections; but in the light of subsequent experience, we think that both cases could probably have been correctly diagnosed clinically by the two following points:—

(1) That they had not got the convoluted raised border so characteristic of epithelioma of the cornea and conjunctiva, and (2) apart from the few pink spots seen in Case III—the growths were of the dead-white colour of sodden epithelium, instead of being pinkish white with distinct vessels in the substance of the growth as in epithelioma.

We find great difficulty in classifying these growths satisfactorily. We cannot call them *warts of the conjunctiva*, because they do not show the essential feature of warts, viz., hypertrophy of the papillæ; nor can they be called *corns of the conjunctiva*, as there is no ingrowing process of the epithelium.

They seem to us to correspond most closely with *callosities*

CASE II.

FIG. 4.

CASE III.

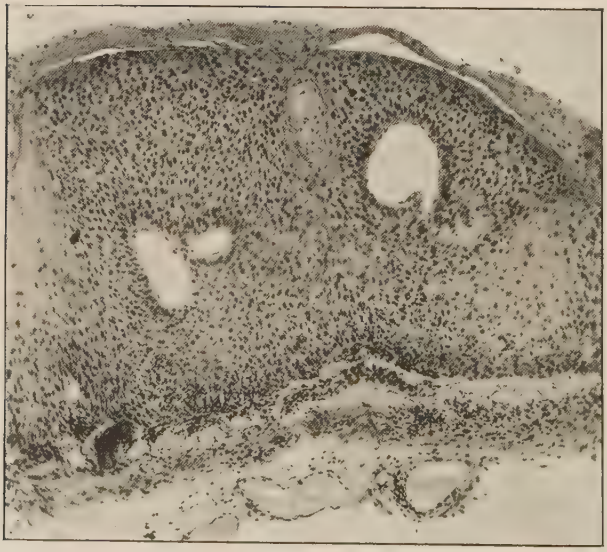

FIG. 5.

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CASE I.

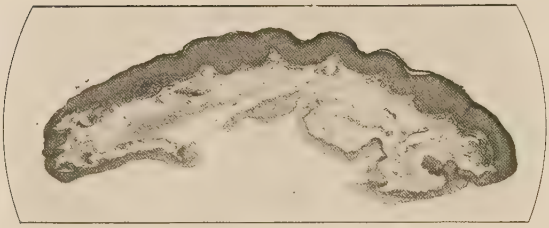

FIG. 1.

CASE III.

FIG. 2.

CASE I.

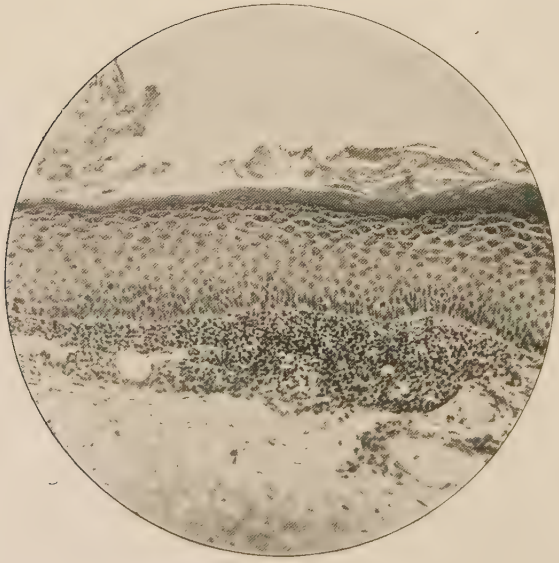

FIG. 3.

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of the skin, which are produced by hyperplasia of the horny layers, and may be either congenital or acquired.

We think that Cases I and II are probably of a different type from III and IV, but till we can gain further information, we class them together under the same title of *epithelial plaques of the conjunctiva.*

In conclusion, we have to thank Mr. Treacher Collins for kindly allowing us to make use of Cases I and II, which came under his care, and Mr. William Lang for allowing us to mention Case IV.

Bibliography.—Beyond the papers already mentioned, we are unable to find any further references to cases similar to those described.

Description of Plates.

Plate 1.

1. Case I.—× 10. Showing papilla and sharp limitation of growth.
2. Case III.—× 15. Showing the great hypertrophy of the epithelial layer; gradual thinning of the edges and the blood vessels embedded in the epithelium. No definite processes of fibrous tissue pass into the epithelial mass and no processes of epithelium pass into the subjacent tissue.
3. Case I.—× 80. Showing the superficial horney layers, stratum granulosum and infiltration of subjacent tissue with small round cells.

Plate 2.

4. Case II.—× 80. Showing the sharply-defined margin of growth.
5. Case III.—× 80. Showing the thin-walled blood vessels embedded in the epithelium and the processes of horny cells passing from the superficial layer into the underlying epithelium.

A PATHOLOGICAL REPORT ON A CASE OF MOOREN'S ULCER OF THE CORNEA.

By W. T. Lister, F.R.C.S.

Through the courtesy of Mr. Lang, I am enabled to bring forward the following case of Mooren's ulcer, which came under his care at the Royal London Ophthalmic Hospital, and to give a pathological report on the condition.

D. H., male, æt. 48, came to the hospital complaining that the R. eye had been painful on and off for 12 months.

There was a mucopurulent discharge on the R. side, and the R. cornea was completely opaque, vascular, and rough. On the inner side of the cornea there was an irregular marginal ulcer with overhanging edges. The vision in this eye was reduced to perception of light only. The L. eye was normal, and vision was 6/6. Owing to the prolonged suffering of the patient, and to the bad state of the R. vision, enucleation of the R. eyeball was performed.

On section of the eye, after fixing and freezing, the anterior chamber was found normal and the pupil was free; the lens and vitreous were clear; and the retina and choroid were *in situ*. Microscopic sections of the cornea were made, which show well the peculiar characteristics of this form of ulceration.

The most striking features of the ulcer itself are its depth and the undermining of the edges. The depth of the ulcer varies in different places from one-third to one-half the thickness of the cornea. The floor of the ulcer presents signs of interstitial inflammation with vascularity, but the amount of infiltration with small round cells varies considerably; in places the floor is fairly clean, in other parts the corneal lamellæ are covered with a layer of broken-down

tissue densely infiltrated with cells. The deepest layers of the cornea show little or no change.

The extent to which the margins are undermined is considerable, varying from $\frac{1}{2}$ to 1 mm. The anterior lamellæ of the cornea, forming the overhanging edges of the ulcer, consist of about one-third the thickness of the normal substantia propria. The epithelial layer has a very irregular base line, and has to a slight degree grown round the free edge. Bowman's membrane is absent, and the corneal lamellæ are greatly altered from the normal. No definite layers can be made out, several blood-vessels are seen cut across, and there is infiltration with round cells, which in places is very dense.

Over the rest of the cornea, where the ulceration has healed, the epithelium is very irregular in thickness, and in places passes in finger-like processes into the corneal tissue beneath. (The plate shows this feature well, and its likeness to rodent ulcer of the skin is easily seen.) At the base of one of the overhanging edges is an oval mass of epithelial cells. This is evidently due to the ingrowth of epithelium at a neighbouring area of ulceration. Bowman's membrane is completely absent, showing, probably, that the whole surface of the cornea has been invaded at one time by the ulcerative process.

The substantia propria is, on the whole, thinner than normal, and, for the most part, shows very marked interstitial change—formation of new vessels and irregular scar tissue. The deepest layers are more affected in this part than opposite the floor of the ulcer.

The episcleral tissue is intensely infiltrated with small round cells, and the vessels are dilated and engorged with blood. Descemet's membrane and the endothelium are unaffected; the angles of the anterior chamber are open; the iris, ciliary body, and lens show no pathological change.

As is well known, corneal epithelium rapidly covers any irregularity in the surface of the cornea, whether it be a clean operation wound or the necrotic margins of an ulcer,

and it is therefore easy to understand that, with a chronic form of ulceration, the epithelial cells may grow round the free margin into the deeper layers of the cornea—and, after cicatrisation has taken place, the embedded epithelium appears on section in the form of finger-like processes invading the underlying tissue.

Some of the sections show that the ulcer is attacking parts of the cornea which have already cicatrised. This may not be usual, since it is at variance with the rough clinical observation, that the ulceration does not, as a rule, return to a part of the cornea which has once healed.

(A complete bibliography is given in Mr. Nettleship's paper in the "Transactions of the Ophthalmological Society," vol. xxii, p. 103.)

Description of Plates.

Plate 1.

1.—Ulcer as a whole under low power × 15. The separation of Descemet's membrane and the splitting of the substantia propria is artificial.

2.—The overhanging edge of the ulcer × 80. The epithelium is very irregular in thickness and extends round the tip. Beneath there is great interstitial change—infiltration with round cells and vascularisation.

The floor of the ulcer is covered with broken-down corneal tissue infiltrated with round cells. On the right side a round mass of epithelial cells is seen.

Plate 2.

3.—The outer edge of the ulcer × 80, showing greater infiltration with round cells.

4.—Healed portions of cornea × 80, showing the finger-like process of epithelium embedded in the cicatrised substantia propria.

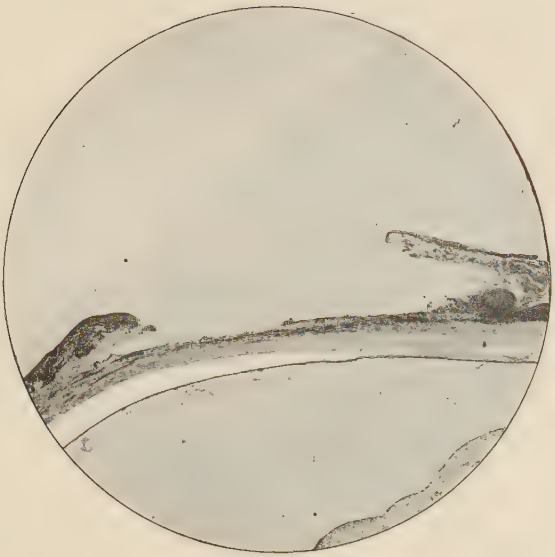

FIG. 1.

FIG. 2.

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Fig. 3.

Fig. 4.

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TWO CASES OF PIGMENTATION OF THE RETINA.

By E. Erskine Henderson, F.R.C.S.

The following cases show different types of pathological pigmentation of the retina, complicated in each case by glaucoma. In the second case there was retinitis pigmentosa in the other eye.

Case I.

E. R. (6,502), female, æt. 72, was admitted to the R.L.O.H. on 18.xii.02, under Mr. Fleming. She had suffered great pain in the R. eye for one month. She stated that the pain preceded the blindness.

18.xii.02.—The R. eye was in a condition of absolute glaucoma and was enucleated.

L. V = 6/24 H.M. 1·75 d. sph. = 6/6; fundus normal.

R. eye was hardened in 10 per cent. formol, frozen, and bisected vertically.

Macroscopic Examination.—The angle of the anterior chamber was blocked by the iris for a distance of about 1 mm., and there was some irregular pigmentation of the fundus.

Microscopical Examination.—Sections cut in celloidin were stained in hæmatoxylin and eosin by Van Gieson's method. Iron was tested for by Perl's ferrocyanide reaction. Sections were also bleached with permanganate of potash and oxalic acid and subsequently stained.

Cornea.—Epithelium, slightly loosened and œdematous; substantia propria and Descemet's membrane show no changes except at the periphery, where the iris is adherent.

Iris.—Thinned, atrophic, and deeply pigmented. Numerous round cells carrying pigment are on the anterior surface and in the substance. It is adherent to the cornea at the periphery for a distance of about 1 mm. Here some pigment is present in the substance of the cornea and in the meshwork between the angle and the canal of Schlemm.

Ciliary Body.—This also is much atrophied; tubular pigmented processes spread out into the vitreous. [Alt. Treacher Collins.][1]

Lens.—This was not examined.

Choroid.—Atrophic. It is very deeply pigmented in places. Choroid and retina are in many places firmly attached, and here Bruch's membrane shows some thickening. Bruch's membrane is, however, intact. The chorio-capillaris is entirely destroyed. The larger vessels show hyaline thickening of the walls and proliferation of the intinia. Some pigment is to be seen in the inner layers of the sclera, chiefly in the neighbourhood of the short posterior ciliary vessels.

Retina.—Almost all trace of the original structure has disappeared. It is much thinned. The connective tissue framework has undergone extensive proliferation. There is no trace of a rod and cone layer. Between the fibres spaces are to be seen containing a granular material, staining faintly with eosin. Numerous round nuclei are scattered irregularly throughout the entire structure. The pigment epithelium is sometimes depigmented, sometimes wanting, and in other places has proliferated. From these latter places processes are to be seen running into the retina, especially in the neighbourhood of the larger blood vessels. The pigment is mostly intracellular, but numerous fine granules lie free in the tissue. Only in a few places does the pigment pass beyond the hyaloid and form a layer on its inner surface, as in the cases described by v Hippel[(2)]. In other places there are a few free red blood corpuscles lying on the inner surface of the hyaloid. The walls of the larger blood vessels show much hyaline thickening; in some the lumen is apparently obliterated. These changes affect the whole retina, but are more marked at the posterior pole. All the pigment is bleached by the method described, and no iron reaction is obtained.

Case II.

D. F. (6,522), male, æt. 21, was admitted to the R.L.O.H. on 17.xii.02, under Mr. Lawford.

L. eye had been blind for some years, but had recently been getting larger and painful. It was in a condition of absolute glaucoma. The cornea was opaque, and there was a ring of ciliary staphyloma.

R. V = 6/60 unimproved—corneal nebulæ—nystagmus—shallow A.C. Pigment on lens capsule. The fundus showed the appearance of retinitis pigmentosa. There was a history of nyctalopia of at least 5 years' duration.

17.v.02.—The L. eye was enucleated and prepared for examination in the same way as the first case.

Macroscopic Examination.—The cornea is opaque and thickened There is a ring of ciliary staphyloma. An anterior synechia is present. There are pigmentary changes in the fundus.

Microscopic Examination.—Cornea. This is in a condition of pannus degenerativus. The epithelium is much thickened, and the superficial cells in many places considerably flattened, but all possess nuclei. Vessels of new formation are present in the deeper layers. Bowman's membrane has almost entirely disappeared. The substantia propria contains numerous vessels, and is infiltrated with small round cells. Descemet's membrane is much thickened, and in the neighbourhood of the anterior synechia appears to split into two layers. The endothelium has in some places proliferated and in others has disappeared.

Iris.—Deeply pigmented on the posterior, but deficient in pigment on the anterior surface. Foci of small-celled infiltration are present. A few large hyaline cells, staining deeply with eosin, are present. The pupil is blocked by an endothelial-clad membrane, which extends up to the anterior synechia and becomes continuous with it. The endothelium is probably derived from Descemet's membrane.

Lens.—The capsule at the anterior pole is much thickened and the epithelium has proliferated to form an anterior capsular cataract. The lens fibres underlying are vacuolated and swollen near the equator; the iris is adherent to the lens capsule. The capsule at the posterior pole is much thickened, and here also there is vacuolation and separation of the lens fibres, forming a posterior polar cataract.

Choroid.—Much atrophied; the chorio-capillaris has practically disappeared. The larger vessels show considerable hyaline thickening of their walls and proliferation of the intima. Bruch's membrane is everywhere intact, but shows occasional thickenings.

Retina.—This is partly detached from the choroid as a result

of the hardening process. In some places it is still firmly attached, without any definite fibres passing from one to the other. The neuroglia has largely proliferated, forming a network with spaces containing round cells and some structureless, slightly granular material. Over the greater part of the retina only one nuclear layer is to be recognised. This, on being traced to the macula, evidently corresponds with the inner nuclear layer. Only in the immediate neighbourhood of the macula is a definite rod and cone layer still preserved. In the rest of the retina the outer layers are fused into a fibrous meshwork with arcade-like spaces containing round cells, pigment and finely granular material. The pigment epithelium has in places proliferated, is absent in others, and in yet others has lost its pigment. Processes from the proliferated pigment epithelium pass into the retina and proliferate in the neighbourhood of the larger vessels. The pigment is for the most part intracellular, but also lies free in the form of fine granules in the previously noted fibrous meshwork. The blood vessels are much altered. The walls are thickened and hyaline, the intima has proliferated, and in some the lumen is obliterated and filled with pigment. The optic disc is cupped, but there is not much development of fibrous tissue. As in the preceding case, all the pigment is bleached, and no iron reaction is obtained.

The pathological changes in these two eyes correspond fairly with the classical descriptions of retinitis pigmentosa (Ginsberg).[3]

The first case differs in some respects, notably in the excessive choroidal changes. The fact also of the other eye being free from pathological change, makes the diagnosis of retinitis pigmentosa very improbable. The case was probably one of chorio-retinitis. Stein,[4] in a paper on the pathological anatomy and differential diagnosis of syphilitic chorio-retinitis, describes four cases, two of which were cases of retinitis pigmentosa and two were cases of syphilitic chorio-retinitis. He points out that in both affections we have to do with a somewhat similar change in the choroid and retina, and that this, in his opinion, is due to a wide-

spread sclerosis of the retinal and choroidal vascular system. As points of differentiation, he notes that, in the syphilitic cases, Bruch's membrane is not usually intact, and that the choroid suffers much more than in retinitis pigmentosa. In the latter Bruch's membrane is always intact.

The second case in all probability was one of retinitis pigmentosa.

In both cases there are very extensive changes in the choroidal vessels. They would thus tend to support the theory that attributes the origin of pigmentary changes in the retina to interference with the choroidal circulation. In this connection the experiments of Wagenmann[5] are of importance. In his experiments rabbits were used. He divided various ciliary and retinal vessels, and made careful opththalmoscopic and microscopical examinations of the changes that ensued.

The experiments that chiefly bear on the points at present under discussion were those in which one long ciliary and some of the posterior short ciliary branches on the same side were divided. Half-an-hour after the section an opacity begins to appear in the periphery of the retina of the half whose circulation has been interfered with. In 6 hours this has spread over the whole half retina and remains unchanged for 2 days. As it begins to recede, the retina, owing to folds, shows network-like markings, and fine spots of pigment make their appearance.

From the 5th day onwards larger clumps of pigment are to be seen. The retinal vessels remain normal. After the 4th week some slight atrophy of the nerve is apparent, but is not marked. Later, anterior and posterior polar cataracts are met with. Microscopically, in the early stages there is general serous œdema of the retina, and the outer layers are separated by a finely granular albuminous material; after the 2nd day the rod and cone layer disintegrates. The pigment epithelium in places disappears, and in places proliferates and sends processes into the retina. The retina later becomes very thin and atrophic. No pigmentary

changes follow interference with the retinal vessels. In discussing the bearing of these experiments, the author points out that, owing to the difference between the retinal blood supply in man and the rabbit, too close an analogy must not be drawn (Parsons).[6] In a subsequent paper[7] the same author describes the microscopical anatomy of a case of retinitis pigmentosa, in which the changes in the choroidal vessels support his view. A similar case is reported by Bürstenbinda.[8]

In this case, however, a perforating corneal ulcer had started a panophthalmitis, to which some of the changes observed in the choroid may have been due. Nettleship[9] has pointed out that the somewhat less efficient blood supply to the equator of the eyeball may determine the starting point of the disease. It is difficult, however, to see why the subjects of this disease, if it was entirely due to vascular disturbance, should have only the choroidal vessels affected, and not those in other parts of the body.

Another point of interest in these two cases lies in the possible relation between the retinal and choroidal changes and the glaucoma. E. v. Hippel (*loc. sup. cit.*) reports two cases of glaucoma in which pigmentary changes were found in the choroid and retina. In these, although the angle was free, the fibrous mesh-work between it and Schlemm's canal was filled with pigment cells. He suggests that the pigment cells may stop the filtration process, and that, as happened in his cases, neither myotics nor operative measures will effect a reduction of tension. He quotes similar cases recorded by Priestley-Smith,[10] Alt[11] and Dolganoff.[12] He also points out that pigmentary changes in the retina, similar to those in retinitis pigmentosa, may be present without change in the choroidal vessels as a result of a chemical influence, *e.g.*, a splinter of iron. In neither of the two cases here reported was there much pigment in this situation.

Weiss[13] instances a case of retinitis pigmentosa complicated by glaucoma, and collects from the literature of the

subject 17 others. He points out that it is possible that the cases of glaucoma complicating retinitis pigmentosa are more common than is supposed. Patients with an incurable disease like retinitis pigmentosa drift out of observation, and even if later attacked by glaucoma, attribute this to the original complaint, and as they are already blind do not again appear for inspection.

In the Clinic at Giessen, out of 55 cases of retinitis pigmentosa observed since 1890, only one was complicated with glaucoma.

Birnbacker and Czermak[14] have suggested that an inflammatory process in the choroid may lead to blocking of the venæ vorticosæ and so to glaucoma.

That a similar predisposition to vascular changes may underlie both complaints is suggested by a paper by Blessig.[15] An account is here given of a family of nine, in which two sisters suffered from glaucoma and two brothers and one sister from retinitis pigmentosa.

Bibliography.

(1.) Alt. Compendium. New York, 1880; Treacher Collins. Researches. London, 1896.
(2.) E. v. Hippel. Arch. f. Ophth., Bd. lii, p. 498.
(3.) Ginsberg. Grundriss der pathologischen Histologie des Auges. Berlin, p. 341.
(4.) Stein. Arch. f. Ophth., Bd. lvi, 3, p. 463.
(5.) Wagenmann. Arch. f. Ophth., Bd. xxxvi, 4, p. 1.
(6.) Parsons. The Ocular Circulation. London, 1903, p. 18.
(7.) Wagenmann. Arch. f. Ophth., Bd. xxxvii, 1, p. 230.
(8.) Bürstenbinder. Arch. f. Ophth., Bd. xli, 4, p. 175.
(9.) Nettleship. R.L.O.H. Reports, vol. xv, pt. 3, p. 195.
(10.) Priestley-Smith. Path. and Treatment of Glaucoma, p. 54.
(11.) Alt. American Journal of Ophth., 1896, p. 296.
(12.) Dolganoff. Arch. f. Augenheilk., xxxix, p. 129.
(13.) Weiss. Retinitis pigmentosa und Glaukom. Halle, 1903.
(14.) Birnbacker and Czermak. Arch. f. Ophth., xxxi, i, p. 297.
(15.) Blessig. St. Petersburger Med. Wochenschrift, 1902; quoted in Centralblatt f. Augenheilk. Supplement, 1902, p. 476.

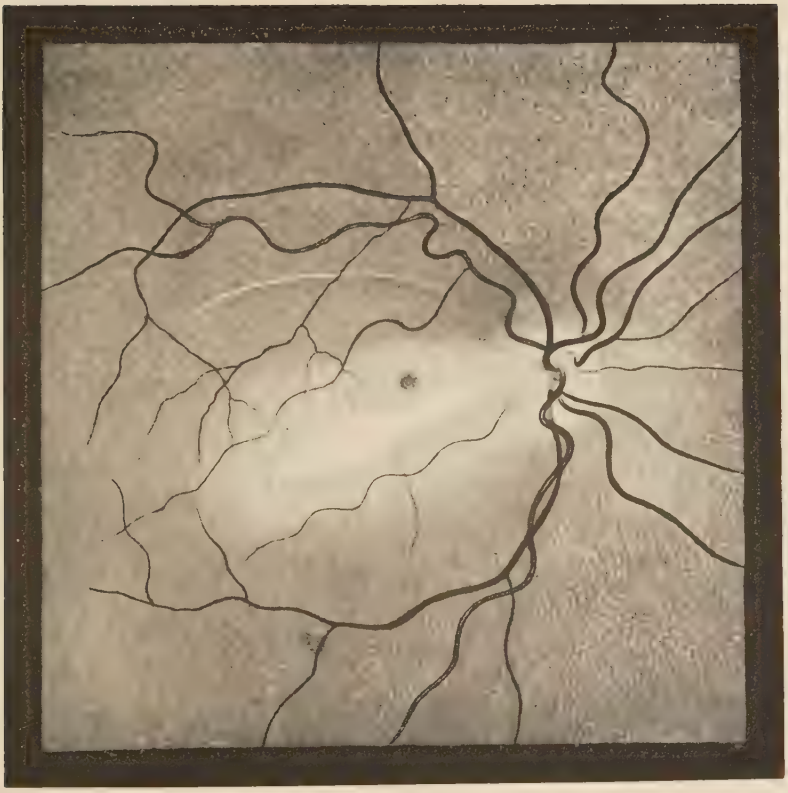
I. A CASE OF ORBITAL WOUND IN WHICH THE OPTIC NERVE AND CENTRAL RETINAL VESSELS WERE DIVIDED.

By J. Herbert Parsons, *Curator*.

Records of cases of division of the optic nerve anterior to the entrance of central retinal vessels are rare. Such cases present ophthalmoscopic appearances which are characteristic, and are of diagnostic importance.

Henry Aston, æt. 28, was stabbed in the R. eye with a table-knife on 1.ii.1903. He was treated by Dr. Herbert Hall at the Watford Hospital on the same night. The eye was protuberant, of stony hardness, and quite blind. No temperature developed, the swelling went down, and the tension steadily diminished.

9.ii.1903. Patient admitted to R.L.O.H., under Mr. Lang. There was a wound in the lower lid just below the inner canthus. The eye movements were good in all directions except outwards, the external rectus being paralysed. Slight proptosis. There was extensive subconjunctival hæmorrhage on the outer side. The cornea was anæsthetic; a.c. normal. The pupil was dilated, did not react directly to light, but gave very slight movements in the lower and outer quadrant on consensual stimulation. On ophthalmoscopic examination a large area of œdema was found at the posterior pole; it extended farthest on the outer side, where it reached two-thirds of the distance towards the periphery. The optic disc was pink, with a well-defined physiological cup; the edge of the disc was blurred. The vessels were of good size, the veins slightly larger than the arteries, and both were of nearly the same colour, which resembled that of normal veins. They could be traced to the bottom of the cup, with little variation in size. There was no spontaneous pulsation in either arteries or veins. On moderate pressure by means of the finger upon the globe, the blood could be driven out of both sets of vessels towards the disc. The blood in them was therefore under much reduced intravascular pressure, and the circulation must have been



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extremely sluggish if present at all. A dense opaque white area extended outwards and a little downwards from the outer edge of the disc to beyond the position of the macula, measuring three discs' diameter horizontally, and half a disc's diameter vertically. The edges were sharply defined, and greenish-white; they were less well defined at the inner and outer ends, shading off here into the surrounding œdematous retina. The surface of the patch could be seen with + 2 D, the rest of the fundus being emmetropic, but measurement could not be made absolute as there were no vessels, &c., upon the surface. There was a small, irregular, stippled red spot above the inner end of the white patch, at about a diameter and a half from the disc. The small vessels near the patch were irregular in calibre; they disappeared at the margin of the patch, except at the outer part, where they could be traced as fine lines, often broken, over the surface. Vision, nil; tension normal.

12.ii.03. Appearances much the same. The vessels empty rather less easily on pressure.

13.ii.03. Consensual pupil reaction down and out confirmed by several observers. Slight pressure on the globe produces arterial pulsation, rather more empties the vessels. The similarity in colour of the arteries and veins is slightly less marked. The red spot above the white patch is undoubtedly a punctate hæmorrhage.

16.ii.03. There are many small punctate hæmorrhages, especially beyond the outer end of the white patch. The œdema is clearing up considerably, and does not extend far beyond the patch; the periphery of the fundus looks quite normal. There are vessels on the white patch, with short broken columns of stagnant blood. There is also an appearance of fresh vessels here.

19.ii.03. The pupil contracts with $\frac{1}{4}$ per cent. eserin.

20.ii.03. The œdema has almost disappeared. The white patch is covered with small broken vessels, containing very dark blood. A thin white film passes over one of the lower macular arteries. The hæmorrhages have disappeared. Patient discharged.

5.iii.03. Cornea anæsthetic; small ulcer on outer side, which stains with fluorescein; ciliary injection. Pupil semi-dilated. Slight tendency to ectropion of lower lid opposite site of wound.

16.iii.03. Ulcer *in statu quo*. Ophthalmoscopic examination difficult. The retinal vessels were seen to be irregularly full; some veins were larger, others smaller, than the corresponding arteries; none were fully distended. Fundus bluish, with stippled appearance over the area outside the disc. There is a network of small vessels over the area which was formerly white. No hæmorrhages.

7.v.03. Movement of the eye outwards is now almost full. Ulcer still stains; cornea anæsthetic. Pupil dilates more above than below. Optic disc very pale, obviously atrophic. Retina slightly hazy. Macular region now red, with a spot of pigment at the macula.

18.v.03. Ulcer healed.

4.vi.03. Cornea still anæsthetic. No p.l.

20.vii.03. Eye movements good in all directions, not quite full outwards. Cornea anæsthetic, nebula. Iris immobile; pupil 4 mm. in diameter. Optic disc chalky-white. Arteries and veins equal and small, rather dark, with very little difference in colour, but quite distinguishable. Retina good colour, but much degenerated, showing increase of fibrous tissue. There is a small black ring at the macula. No p.l.; tension normal.

Wounds of the optic nerve have been discussed, *inter alia*, in the monographs of Yvert (1880) and Praun (1899). I propose to consider only those in which the nerve was divided anterior to the entrance of the central retinal vessels.

v. Graefe (1859) reported the case of a student who received a wound from a duelling sword (Schläger). The eye was blind, and ophthalmoscopic appearances resembled those of embolism of the central artery. v. Graefe diagnosed tearing of the central vessels.

H. Pagenstecher (1869) gave a very detailed description of the case of a girl, æt. 12, who was wounded by the sharp iron point of a bar (Stange). Seen on the 4th day after the injury, there was complete amaurosis. Instead of the usual red reflex, there was a bright white reflex from the widely-dilated pupil. The disc was only recognisable by a blood

vessel which ran downwards for a distance less than a papilla-diameter. The vessel contained blood at intervals, was irregular in diameter, and it was uncertain whether it was an artery or a vein. A similar smaller vessel ran upwards. The papilla was bright white, the area between it and the macula grey, fading off towards the periphery to red. Observations were continued for 2 months. On the 5th day the œdematous area was larger; a few more vessels were visible. On the 6th day the œdema had diminished, and the edges of the disc were just distinguishable. More vessels were to be seen; they still showed empty spaces. On the 7th day the œdema was still less; the edges of the disc were distinct, but the area between the disc and macula was still sharply limited from the surrounding retina. On the 8th day the vessels were still fuller; some "choroidal" plaques at the periphery showed commencing pigmentation. This pigmentation continued to increase, more and more pigmented areas being developed, so that they encroached on the central areas. The disc became completely atrophic. The blood vessels continued to increase in number and became better filled. It was impossible to distinguish between arteries and veins. Pressure on the globe caused no pulsation. Many of the vessels were obviously of new formation, and not merely the normal ones restored; this was further proved by the development of anastomotic branches. A month after the injury there was no consensual pupil reaction; the pupil contracted under eserin. The vessels were now smaller than before, and pigment was distributed along them in the peripheral parts of their course. There was at this period a distinct extravasation of blood a little above the macula. At a later stage the peripheral ends of the vessels became reduced to bloodless white cords running through bands of pigment. In 6 weeks the white atrophic papilla was partially pigmented and free from blood-vessels. The retinal blood-vessels appeared a short distance outside the edge of the disc; they were much reduced in size.

H. Pagenstecher in the same paper recorded the ophthal-

moscopic appearances in a case of extirpation of an orbital growth, the eye being retained, though the optic nerve was cut through. On the 4th day there was a white reflex, with a few red vessels; the papilla was indistinguishable from the retina. On the 13th day the neighbourhood of the macula seemed to be detached. On the 18th day the disc was reddish, the vessels distinct, but arteries and veins could not be differentiated. The retina around the disc was still greyish-white, and there were deposits of pigment about the macula.

The observations in this case are amplified in a similar one recorded by Knapp (1874). An extradural endothelioma of the optic nerve* (described by Knapp as a carcinoma) was removed from a woman, æt. 40, the globe being retained. On the 2nd day there was a whitish-yellow reflex. On the 3rd day the tension was normal. On the 4th day the central part of the fundus was white, the periphery yellowish-red. On the 5th day two dark red streaks marked the position of retinal vessels: they were apparently veins; they had pointed extremities and no pulsation was visible. On the 6th day the œdematous area showed diminution; the two vessels were longer, and four or five new small ones had appeared. On the 7th day day there were 15–20 vessels, only two of which reached the centre; these were broadest and longest and were very wavy. The general appearance resembled embolism of the central artery of 5 or 6 days' duration. On the 8th day the contours of the disc were dimly visible, and arteries and veins could be differentiated. On the 9th day venous hyperæmia was more pronounced; there was no pulsation on pressure; there was no dark red spot at the macula. From the 10th to the 12th day the œdema diminished and the venous hyperæmia increased. On the 15th day the latter was very striking, the veins being varicose at the disc. This condition increased still further, with the development of extensive extravasations of blood. Still later the hyperæmia gradually diminished, the disc became pale, and the vessels

* See Parsons, Trans. Ophth. Soc., vol. xxiii, 1903.

were reduced to white strands. The hæmorrhages were replaced by pigment. The author gives three most instructive ophthalmoscopic plates, showing the appearances before operation (optic neuritis), and 3 weeks, and 7 months after operation.

Just (1873) reported a case briefly; red vessels were seen, on a bright white ground, on the 3rd day after the injury. It is improbable that the vessels were divided in this case.

Hirschberg (1879) saw a patient whose optic nerve and central vessels had been divided by a splinter of wood 4 weeks before. There was a bluish mass in the vitreous, probably following hæmorrhage. The retina, where visible, showed hæmorrhages and streaks of pigment.

Aschmann (1884) recorded two cases. In the first, due to injury with a bean-prop (Bohnenstickel), the optic nerve was torn from the retina. The site of the disc looked grey, and formed a deep cup. In the second case, due to a blow with an umbrella, the disc was covered with blood clot, the retina was detached, and the choroid ruptured. After enucleation it was found that the posterior part of the globe was torn.

Karafiáth's case (1884), due to a revolver shot, 22 days after the injury showed blood in the outer half of the vitreous and cupped steel grey papilla, without vessels. Around the disc was a yellowish-white area, reaching almost to the equator on the temporal side, sprinkled with bright and dark brown spots. Beyond this were many hæmorrhages; some dark vessels could be seen only on the nasal side.

Schliephake (1888) reported a case of injury with a billiard cue. The fundus was grey, the papilla hazy, without vessels. The vessels filled up and became congested, but were again scarcely visible after 6 weeks, when the fundus was pigmented.

Liebrecht (1891) recorded a case of partial section of the optic nerve, including the central retinal vessels, by

a piece of glass. The whiteness of the fundus is noted, and the narrowness of the arteries after a few weeks. There was also pigmentation. The early stages could not be observed.

Blessig (1898) reported two cases: (1), Seen on the 2nd day, showed œdema of the retina, arteries narrow, veins beaded, red spot at macula, and after 10 days, disc atrophic, arteries narrow. (This is a doubtful case.) (2), Seen after 4 weeks, showed vitreous opacity, disc pale, vessels narrow, œdema of macula, with red spot.

Mendel's case (1899) gave the picture of embolism of the central artery, and ended in optic atrophy.

Neuburger (1901) recorded a case due to fall on a stick. Seen on the 3rd day, there was œdema of the disc and retina; no arteries were visible, and the veins were irregular. After $3\frac{1}{2}$ weeks the nerve was atrophic, the retinal vessels were partially restored, the œdema had disappeared, and there was a rupture of the choroid.

Birch-Hirschfeld (1902) has reported the most recent case. A boy, æt. 13, was wounded with a hay fork. The case was observed from the 4th day to the end of 3 months after the injury. On the 4th day the tension was diminished; the retina was hazy, with hæmorrhages, chiefly near the nasal side of the disc; the disc was replaced by a hole, due to the nerve having been torn out of the sclerotic; a small vessel disappeared over the edge down and out; other rudimentary vessels were only to be seen at the periphery (Dr. Zetzsche). On the 13th day the cornea was sensitive; pupil was widely dilated, and there was no consensual reaction. The situation of the disc showed a deep cup (−6 D), and was bluish-grey with an evident shadow. The edge of the disc was slightly raised, and showed whitish spots and stripes. The retinal vessels looked fairly normal, of medium size. The area between the disc and to two papilla diameters beyond the macula was grey, fading off into the normal retina outwards and above, but limited below by a narrow area of hæmorrhage. In the next 4 days

the œdema at the posterior pole cleared considerably, but was still visible on the 21st day. In the course of the following 2 months, the cup at the position of the disc became filled with white fibrous tissue, and bands of the same material replaced the hæmorrhagic area, with the exception of a dark red spindle-shaped patch. The fibrous tissue at the disc sent bands forward into the vitreous. There was a little pigmentation below, and less above, the disc.

Division of the optico-ciliary bundle experimentally was first investigated by Berlin. He operated upon rabbits, and found very extensive œdema of the whole retina. Leber confirmed the results in the cat. It is not easy to divide the central vessels in lower mammals, as they enter the eye close to the sclerotic.

The experiments were extended by Krenchel, who operated on frogs, and the whole subject was very exhaustively investigated by Wagenmann. The latter found that simple section of the nerve and central vessels did not cause retinal œdema, but this followed section of the ciliary arteries only. This observation requires confirmation. Wagenmann also attributes the pigmentation of the retina to injury of the ciliary blood supply.

A review of the cases presents a very constant group of ophthalmoscopic signs, which are of extreme diagnostic and pathological interest. Many of the signs, such as disappearance of the vessels, temporary diminution of intraocular tension, &c., are only what might be expected. Two features demand special consideration: (1) Œdema at the posterior pole; (2) re-vascularisation of the retina.

Œdema at the Posterior Pole.—The occurrence of œdema in tissues deprived of their blood-supply is exemplified in many conditions in various parts of the body, and need, therefore, occasion no surprise in the retina in such conditions as embolism of the central artery or section of the optic nerve anterior to the entry of the central retinal vessels. Anæmic tissues take up fluid with great avidity,

and this is doubtless due to the alteration in osmotic pressures brought about by the retention of katabolic products, though the exact rationale of the phenomenon has yet to be worked out.

It is less easy to understand why the macular region should suffer in so disproportionate a degree. The resemblance of the ophthalmoscopic picture in these wounds of the nerve to that of embolism has been pointed out by several observers. There can be little doubt that the cause is the same in both conditions. Direct injury of the posterior pole of the eye can be definitely eliminated in several of the cases, as in that recorded here. In the wounds of the nerve the whole retina would probably be found to be œdematous in the very earliest stage a few hours after the injury; if not, it must be due to the comparatively free vascularisation of the anterior part of the choroid by the recurrent branches of the anterior ciliary vessels. The exact parallelism between the œdema of the macular region in embolism and that in the condition under consideration is found in the fact that in the latter the macular region is the last to clear up as the retina becomes revascularised. This depends, I believe, upon the fact that, *quâ* retinal blood supply, this area is worst provided for. Hence, as the circulation is re-established, effete material will stagnate there longest, and we have seen that this is the most probable cause of the œdema.

It has already been noted by H. Pagenstecher, in his second case, that the neighbourhood of the macula seemed to be detached. I think it is probable that there was an actual slight detachment of the retina in this situation in the case recorded above. In the earliest condition the bright white summit of the area afforded no means of accurately measuring its position relative to that of the surrounding retina, which, it must be remembered, was also swollen. After the development of new vessels, the difference in height was too slight to authorise a dogmatic statement. Such detachment, if present, was due to the accu-

mulation of fluid under the retina at the most œdematous part. This may account for the absence of a cherry-red spot, but there are other reasons for this. It will be noted, in the cases previously reported, that such a spot is seldom present, though it may be simulated by a hæmorrhage, as in my case. It is mentioned in Blessig's first case, but the condition here of the vessels on the 2nd day is scarcely consistent with division of the central trunks behind the globe.

Reported cases of embolism seem now to have proved conclusively that the red spot at the macula may be due to hæmorrhage, though in most cases hæmorrhage is absent. It would be interesting to discuss the cause of the hæmorrhage when it occurs, but this is beyond the scope of the present paper. When it is absent we must fall back upon the theory of the contrast of the choroid, seen through the thin retina at this spot, with the surrounding œdematous, non-vascular retina. And this is a good reason why there should be no red spot when the optico-ciliary bundle is divided, even if the retina is not actually detached. Under these circumstances the choroid must be almost emptied of blood, the large veins being submitted to the intraocular pressure, and thus emptied. Some blood will still enter the choroid from the recurrent branches of the anterior ciliary vessels, but the choroid at the posterior pole of the eye will certainly suffer most, and we must remember that the partial anterior ciliary blood supply will prevent the intraocular tension from falling to zero.

Revascularisation of the Retina.—No refilling of the retinal blood vessels can occur until the cut ends of the central vessels behind the globe are sealed up. This doubtless happens quickly through retraction and clotting. As soon as organisation is sufficient to withstand the low venous pressure, the vessels will commence to refill through the direct and the indirect cilio-retinal anastomoses near the optic disc.* These anastomoses are rather venous than

* See Parsons, The Ocular Circulation. London, 1903.

arterial; hence the veins will fill up first. This is what we have seen actually occurs, and it takes place on the 4th or 5th day. The blood is, of course, derived from the recurrent branches of the intact anterior ciliary arteries, and also from any posterior ciliary arteries which may have escaped section. The retinal arteries probably fill up first from the periphery, the blood trickling in in the wrong direction from the already refilled veins.

As soon as a few vessels have been refilled, new capillaries will be actually created in these areas. The conditions are exactly similar to those which obtain in the vascularisation of an organising clot, &c., with the exception that the inert mass in the present instance already contains pre-formed blood channels. In both cases there is the requisite stimulus for the proliferation of the capillary walls, new endothelial tubes are formed, and these later put on adventitial sheaths, and so anastomatic branches are formed. In this manner, by the continual opening up of the old paths and formation of new ones, the circulation is re-established. The reverse current in the retinal vessels, if it occurs, is probably of short duration, the arterial anastomoses developing rapidly under their greater internal pressure, so that a normal current is set up.

How does the blood escape from the eye? The answer to this question also explains the occurrence of venous hyperæmia and hæmorrhages. The retinal blood can no longer return by the central vein, which is now quite sealed up. It has to pass out by the same anastomoses round the disc. Here it enters the choroidal veins, is carried forward to the venæ vorticosæ, and so escapes. It is obvious that this circuitous course must offer great resistance to the exit of the blood. Further, the more blood that enters the retinal vessels, which are now, moreover, increased in number beyond the normal, the more difficult will it be for the blood to escape. It is naturally forced on by the high arterial pressure into the capillaries and veins; these become

more and more congested, until finally the weaker ones give way, and extravasations of blood take place.

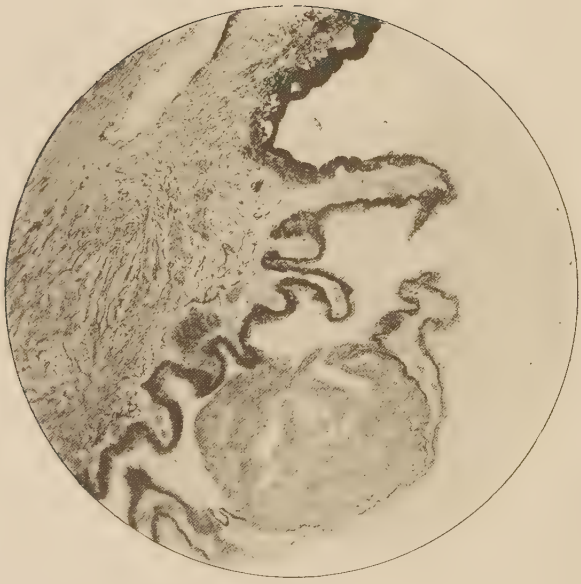
This we have seen to be the actual course of events in some of the cases, but not in all. The reason is not far to seek. The retina has ceased to be a functioning organ; it is now little more than an organising scar. The changes which occur in the new-formed blood vessels, leading to the formation of a connective tissue sheath, do not stop at that point, but go on to the generation of fibrous tissue which replaces the old retinal structures, and eventually, by its contraction, throttles the vessels which produced it. Whilst the process of revascularisation seems to proceed at a very constant rate in all the cases recorded, the process of organisation, which is to be regarded as antagonistic, seems to vary greatly, both in rapidity and in amount. These variations must depend upon the very complex conditions of the individual cases. Hence, in one case we get venous hyperæmia and hæmorrhages; in the other these may be reduced to a minimum, though they are apparently never absent. In the latter event, a moderate hyperæmia passes gradually and almost unnoticeably into anæmia, with narrow vessels which are soon obliterated. The ultimate effect is the same; the retina is transformed into fibrous tissue, in which pigmented areas mark the sites of former hæmorrhages.

Finally, a few remarks may be made about the special case under consideration. What happened is probably as follows:—The knife entered at the lower and inner angle of the orbit, and passed between the internal and inferior recti, pushing these aside without seriously injuring them. It is astonishing how structures may escape a large weapon in this manner, and it would be hardly conceivable if it were not confirmed by innumerable similar cases. The knife then passed on, cutting or tearing through the whole optico-ciliary bundle, with the exception of a few short posterior ciliary vessels and nerves on the lower and outer side. That these escaped is proved by the persistence of the con-

sensual pupil reaction in the lower and outer part of the iris. The section of the nerve is proved by the blindness, absence of direct pupil reaction, and subsequent optic atrophy. The knife, being directed up and out, then caught the VIth nerve on the inner and upper part of the external rectus, near the back of the orbit, and partially or completely divided it. It is unlikely that the muscle was divided, both on account of the nature of the injury and the return of function. For the latter reason it is probable that the nerve may have been merely bruised.

Bibliography.

Yvert. Traité des Blessures du Globe de l'Œil. Paris, 1880.
Praun. Die Verletzungen des Auges. Wiesbaden, 1899.
v. Graefe. Arch. f. Ophth., v, 1, 1859.
H. Pagenstecher. Arch. f. Ophth., xv, 1, 1869.
Knapp. Arch. f. Augenheilkunde, iv, 1874; Arch. of Ophth., iv, 1874 (translation).
Just. Klin. Monatsbl. f. Augenheilkunde, xi, 1873.
Hirschberg. Arch. f. Augenheilkunde, viii, p. 169, 1879.
Aschmann. Dissertation. Zürich, 1884.
Karafiáth. Nagel's Jahresbericht, p. 696, 1884.
v. Hippel. Berl. klin. Wochenschrift, 1886.
Schliephake. Dissertation. Giessen, 1888.
Liebrecht. Klin. Monatsbl. f. Augenheilkunde, xxix, 1891.
Blessig. Nagel's Jahresbericht, p. 865, 1898.
Mendel. Berl. klin. Woch., 1899.
Neuburger. Münch. med. Woch., 1901.
Birch-Hirschfeld. Klin. Monatsbl. f. Augenheilkunde, xl, 1902.
Berlin. Klin. Monatsbl. f. Augenheilkunde, ix, 1871.
Leber. In Graefe-Saemisch, Handbuch, v, 1876.
Krenchel. Arch. f. Ophth., xx, 1874.
Wagenmann. Arch. f. Ophth., xxxvi, 4, 1890.



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II. EPITHELIAL HYPERPLASIA OF A CILIARY PROCESS.

The following case is of pathological interest from the point of view of epithelial growths of the ciliary body. It is almost identical with an "epithelial tumour of the ciliary process" described by Hanke (*v. infra*).

A man, æt. 65, was admitted to the R.L.O.H., under Mr. Holmes Spicer, the left eye having become inflamed 12 days previously. There was no history of injury. The conjunctiva showed intense chemosis; there was a large area of ulceration of the cornea, and this steadily advanced whilst under observation. R. V = 6/36.

It is unnecessary to enter into details of the clinical condition, since the swelling on the ciliary process was probably quite independent of it.

Pathological Examination: Macroscopic.—Large ulcer of cornea with infiltration around. A.c., full of yellow coagulum.

On section in a sagittal direction, an anterior synechia of the iris was noted. The lens was normal, and the retina and choroid were *in situ*.

Microscopic.—Cornea, nearly the whole surface ulcerated; upper and central part entirely necrosed; surface of lower part densely infiltrated in anterior layers. Bowman's membrane is seen for a short distance below; Descemet's membrane extends rather farther below, and is seen for a short distance above. A.c., full of fibrinous coagulum, containing leucocytes; both angles full of leucocytes. Iris, acute purulent iritis; pupil is adherent to slough. Retina and choroid, *in situ;* show congestion and some infiltration.

On one ciliary process below is a globular mass on the anterior surface, with its long axis in the direction of the process. It is about 1 mm. long by 0·75 mm. wide. The non-pigmented retinal epithelium can be traced on to its surface, whilst the pigmented epithelium is continued under it, though the cells soon lose their pigment, which is also absent or scanty on many of the processes.

The main mass of the swelling consists of irregular groups of cells resembling the non-pigmented epithelium, lying in a hyaline matrix, with numerous irregular spaces. The nuclei stain faintly, are round or oval; the outlines of the cells are indistinct. No tubular arrangement of the cells can be demonstrated, though the general disposition is suggestive of such an arrangement.

It is clear, I think, that these cells are due to the proliferation of the non-pigmented or inner layer of the retinal epithelium, and that the proliferation has taken place into the vitreous body, the underlying ciliary process showing the same condition as the others. There is no evidence of inflammation, such as infiltration with leucocytes, either in or around the mass.

The only case on record which at all nearly resembles this one is that of Hanke from Fuchs's clinic. The patient in this case was a woman, æt. 65, and the tumour was similarly met with by accident, the eye being examined for the sake of a pterygium. The swelling was reniform and was covered by both layers of epithelium, though this seems doubtful, both from the figures and the description. In any case, the growth was developed from the non-pigmented layer, and consisted of bands and nests of epithelial cells forming a coarse network. As in my case, the contours of the cells were obscure, the protoplasm having run together into a homogeneous mass, in which the nuclei were embedded.

Hanke discusses the nature of the growth. He regards it as most allied to the epitheliomata. Against this view he mentions the absence of a connective-tissue stroma, and the development of communicating spaces. The first difference is explained by the growth outwards into the vitreous; the second by the specific function of the epithelium of the ciliary processes as a secreting organ.

The absence of tubules, the bands of cells having no lumina, is held to negative the diagnosis of an adenoma of Treacher Collins's glands of the ciliary body, as well as the position of the growth in a ciliary process and its origin from the inner non-pigmented layer.

I think it most probable that both growths are due to chronic degenerative hyperplasia of the epithelium in old age. In Hanke's case the eye was practically healthy, and in mine the disease which led to removal must be looked upon as entirely independent. There are many reasons against regarding the growth as an epithelioma in the ordinary sense of the term. There is no evidence of malignancy, and proliferation is entirely localised, and in a direction outwards. There is no tendency to invasion of other tissues. It might much more reasonably be regarded as a papilloma, and compared with the warty growths which are so common in old age.

Proliferation of epi- and endo-thelium is found in many parts of the eye in old age, and often leads to the formation of warty excrescences. Examples are found in the warty excrescences on Descemet's membrane, more particularly at the periphery. These are undoubtedly due to proliferation of the endothelium and deposition of a hyaline material similar to the membrane itself. More nearly allied to the tumours under consideration are the warty excrescences found on the pars plana in old age. These have been carefully examined and described by Kuhnt and Kerschbaumer. They are due to proliferation of the non-pigmented cells into the vitreous. Neighbouring nodules may cause a festoon-like arrangement. When they are large the central cells may degenerate, and give rise to cysts, which sometimes reach a considerable size.

Similar growths, also in old people, may have a much more pronounced adenomatous type. Such have been described by Pergens and Alt.

The process therefore which gives rise to these unusual growths is essentially degenerative in character, associated with old age. The degenerative changes probably lead to the formation of irritative substances in minute amount, and these stimulate the cells to proliferation. The process is probably extremely slow.

No sharp line can be drawn between these chronic hyper-

plastic changes and the more rapid—but still chronic—ones which lead to the formation of pigmented tubules in cyclitic membranes. Here the irritation is more pronounced, and an essential difference arises in that the epithelium is pigmented, at any rate, in the later stages. (See Treacher Collins.)

Bibliography.

Hanke. Arch. f. Ophth., xlvii, 1899.
Kuhnt. Klin. Monatsbl. f. Augenheilkunde, xix, 1881.
Kerschbaumer. Arch. f. Ophth., xxxiv, 1888.
Pergens. Arch. f. Augenheilkunde, xxxii, 1896.
Alt. Amer. Jl. of Ophth., xv, 1898.
Treacher Collins. Researches. London, 1896.

ACUTE DACRYO-ADENITIS.

By William Inman, Senior House Surgeon, Royal London Ophthalmic Hospital.

Affections of the lacrimal gland have received very little attention from English writers, and literature upon the disease is meagre. The leading text books dismiss the subject briefly. Theobald, in Norris and Oliver's System of the Diseases of the Eye, gives the most complete account of dacryo-adenitis. He divides the condition into two forms: chronic and acute, the latter being very rare. He quotes the following authorities:—

1. Arlt, in his "Lehrbuch," 1853, says he has never seen a case of dacryo-adenitis.

2. Power asserts in the Lancet, 1886, that the indices of the Royal London Ophthalmic Hospital Reports make mention of only one case of abscess of the lacrimal gland.

3. Hirschberg states that among 22,500 recorded cases of diseases of the eye, he met with but one case of suppurative inflammation of the gland.

Power's article, referred to above by Theobald, is a report of a series of lectures on Diseases of the Lacrimal Apparatus, delivered at the Royal College of Surgeons. His observations are to the effect that malaise precedes the signs of local inflammation by one or two days. Then the pain begins in the side of the head, radiating towards the parotid, which is usually swollen and tender. After mentioning the condition of the lid and conjunctiva, he goes on to say that resolution rarely takes place, and that the abscess when formed, bursts into the conjunctival sac, or near the outer angle of the orbit. The disease may occur at any age.

A non-suppurative form of acute dacryo-adenitis, termed "mumps of the lacrimal gland," is, according to Power,

rare, and in the single case there quoted, which was recorded by Hirschberg, it was bilateral.

Theobald goes on to say that the disease is probably less rare that these writers indicate, as the diagnosis is not always easy, being often confused with simple orbital cellulitis. Referring to the acute form, he describes the attack as being usually severe, delirium and cerebral excitement having been noted in some instances. The inflammation very often subsides without the formation of pus. When pus does form, it may discharge through the skin, or into the superior conjunctival *cul-de-sac*. The affection is usually unilateral, but not infrequently both glands are simultaneously affected. The globe may be greatly displaced and its movements restricted and painful. Nettleship (St. Thomas's Hospital Reports, 1877) has met with cases of dacryo-adenitis in which the inflammation was confined to the accessory portion of the gland, the main part not being involved.

Galezowski and C. E. Rider have called attention to the occurrence of the disease in connection with mumps.

Fuchs, in his Text Book of Ophthalmology, says: "It is extremely rare for the lacrimal gland to be the seat of disease. Dacryo-adenitis may go on to resolution; in other cases, suppuration of the gland with discharge of the pus externally has been observed, a fistula remaining afterwards. There have even been described cases of bilateral dacryo-adenitis which ran either an acute or more frequently a chronic course; some of these cases were complicated with simultaneous swelling of the parotid glands."

Swanzy mentions that he has seen one case of acute purulent dacryo-adenitis, but no instance of the chronic affection. When suppuration has taken place the abscess may open into the conjunctiva, as it did in his patient, or through the skin.

Lawson, in his recently published work, considers the chronic form to be more common than the acute. One case of the latter which came under his notice had inflammation

of both lacrimal glands simultaneously, the course of the disease resembling an attack of mumps. He says that cases of acute dacryo-adenitis may suppurate, but gives no indication of the frequency of this complication.

An examination of the Hospital records of the past 10 years shows that not a single case of inflammation of the lacrimal gland was admitted as in-patient during that period until 1901, when one case came under observation. In 1902 several patients suffering from this disease were treated. The number of cases treated as out-patients cannot unfortunately be ascertained, but it is probable that the condition is by no means as rare as described. Appended are notes of 10 cases observed during the past 2 years. They are all classed as acute dacryo-adenitis, since in the majority the inflammation was sufficiently acute to lead to abscess formation, and in those cases where resolution took place, the symptoms are marked by some severity and could not properly be described as chronic. Indeed, no case of chronic dacryo-adenitis has come under the writer's notice.

Gertrude F., æt. 15, became I.P. under Mr. Silcock on May 28, 1901. This case was the first to come under the writer's observation. The notes taken at the time were few, and are only of value in showing that suppuration occurred. It was the discovery of this instance which prompted further investigation of the affection.

The patient attended hospital complaining that the L. eye had become swollen and painful 10 days previously. There was much swelling and induration over the region of the L. lacrimal gland. It was described then as having "a soft elastic feel," and fluctuation was obtained.

Under ether, the abscess was evacuated on the day of admission. Ten days later the patient suffered from an attack of follicular tonsillitis. She was discharged on June 15, when there was still slight discharge from the abscess cavity.

Chas. W., æt. 17, admitted under Mr. Collins, August 26, 1902. Began 14 days ago, as small swelling immediately above the outer canthus. Eyes always normal until that time.

26.viii.02. *Condition on Admission.*—Marked œdema of R. lid, with swelling and induration over the upper and outer orbital margin. Injection and œdema of outer part of ocular conjunctiva. Tenderness on pressure. No proptosis or displacement of globe. Movements of eye not interfered with. Upper lid cannot be raised voluntarily. Fluctuation cannot be made out from external palpation. Temperature 99(2)°. Some malaise. General anæsthetic given. Lid can now be everted with some difficulty, and enlarged gland exposed. Its surface is bluish-purple, and there is much congestion. Fluctuation obtained. Outer canthus slit and gland incised at the most prominent point. Much pus evacuated (about a drachm). Boracic ointment used to protect cornea from the discharge, and irrigations of conjunctival sac with perchloride of mercury, combined with fomentations, ordered.

27.viii.02. Swelling subsiding rapidly. Patient feels much better. Much purulent discharge from gland. Pus oozes from opening when pressure is made through lid. No tenderness. Temperature normal.

31.viii.02. Some thickening above outer canthus persists. Lid now easily and painlessly everted. Gland less swollen. No discharge.

1.ix.02. Thickening of lid disappearing quickly.

Jane C., æt. 3, became O.P. under Mr. Lawson, June 29, 1903. When first seen there were œdema of conjunctiva, suffusion, no discharge, and swelling of the L. upper lid. Impetigo of nostrils was a prominent feature. The child was treated as an O.P. until July 2, 1903, when she was admitted as I.P. under Mr. Collins.

History.—Father says that the child first complained of pain on June 25th. A little discharge from the eye was noticed on the preceding day.

The L. *lower* lid appeared to be slightly swollen, and, on the following day the upper lid became enlarged on outer side, and continued gradually to increase in size. No previous attack, or any other affection of eyes. No recent illness.

2.vii.03. *Condition.*—Whole of upper lid œdematous, fading away on inner side; outer part brawny and indurated. Swelling

limited on outer side by external tarsal ligament. Fluctuation cannot be obtained by external palpation. Palpebral aperture closed owing to thickening of tissues of lid. Some tenderness on pressure. No proptosis. Interval can be felt between the swelling and the orbital margin. No enlargement of pre-auricular gland.

R. lacrimal gland normal. Temperature 97°.

Under chloroform the upper lid can be everted, and the palpebral conjunctiva is seen to be normal.

Lacrimal gland enlarged and fluctuating. Posterior limit cannot be made out.

With finger in upper fornix the lateral boundaries of the gland can be felt, although the surrounding tissues are slightly thickened, as well as œdematous. There is no sign of the abscess pointing at any particular spot.

Gland incised, after having been made to present by pressure externally through lid. About a drachm of thick creamy pus evacuated.

3.vii.03. (18 hours after operation.) Marked improvement in external appearance. Much purulent discharge. Swelling subsiding. No tenderness. Temperature normal.

5.vii.03. Outer portion of upper lid thickened. Very little discharge. There is now no œdema of conjunctiva, and only a little injection at the outer side.

10.vi.03. Gland cannot now be felt through the lid.

Leslie F., æt. 11, admitted under Mr. Tay, August 23, 1903.

History.—The L. eye became inflamed 11 days ago, as if a stye were beginning to form. There was redness at the outer end of the upper lid. No affection of the conjunctiva preceded the attack. The inflammation persisted for a week. The patient was then seen by a doctor, who treated the eye with lotion.

The swelling began to subside yesterday. There was much pain until 3 days ago.

No recent illness. Has never had similar attack before. Had operation for adenoids 6 years ago.

Present Condition.—L. Conjunctiva injected and œdematous, especially on the outer side. Lacrimal gland moderately swollen. Skin of lid over the gland is red and thickened.

Little tenderness. No fluctuation. Gland freely movable, and lid can be everted. There is no evidence of an abscess having opened spontaneously. The vessels on the membrane lining the gland are much distended and tortuous.

Globe freely movable. No proptosis.

There is some chronic marginal blepharitis.

Temperature normal.

24.vii.03. Swelling subsiding, under treatment with fomentations. No tenderness. No discharge from conjunctival sac.

30.vii.03. Discharged. Lacrimal gland is now nearly as inconspicuous as that on R. side.

Jack D., æt. 4½, became O.P. under Mr. Tay, March 16, 1903.

History. Became ill with mumps a week ago. Only L. side affected. The following morning the L. eye became bloodshot, followed 24 hours later by some discharge from that eye, whilst a small lump was noticed on outer part of upper lid. On the 4th day the lid was red, tender, and swollen. This morning an abscess appears to have opened into the conjunctival sac, blood and pus being discharged, causing the pain and tenderness to diminish rapidly.

Present Condition.—There is a localised swelling of outer part of L. upper lid. A central nodule is hard; the surrounding tissues are comparatively soft, and outer margin of induration is limited by the external tarsal ligament. There is very little tenderness. Outer part of ocular conjunctiva is much swollen. No fluctuation. Much purulent discharge oozing from gland can be seen. Pre-auricular gland slightly enlarged and tender. L. parotid gland swollen and slightly tender. The swelling extends backwards behind the ear. Patient can now open mouth widely. Temperature 101°.

17.iii.03. Swelling subsiding, but lacrimal gland is still sufficiently enlarged to prevent examination of orbital wall on outer side with the finger. There is still some tenderness.

23.iii.03. No tenderness. Gland moves freely under the finger. The lid is on a slightly lower level than that of the opposite side, at the outer end.

9.iv.03. Gland not palpable.

4.8.03. Has become O.P. again, suffering from severe

phlyctenular conjunctivitis. There is now no indication of the former inflammatory attack.

Sydney B., æt. 6, became O.P. under Mr. Silcock, April 10, 1902.

History.—L. became inflamed ("like a stye") a week ago. The lid was swollen, and the eye was gradually closed. Two days later the condition was aggravated by blow from brother's knuckle.

Present Condition.—L. Trace of conjunctival discharge. Little swelling and redness of lids (especially the upper one), with an indurated mass at the outer extremity of the upper lid. Much œdema of conjunctiva (ocular) on outer side, a fold being pushed out between the lids. No fluctuation or proptosis can be made out. The swelling is tender, and the lids cannot be separated or everted without much pain. Temperature $99^{(8)°}$.

The mother was ordered to apply fomentations at home. The child was brought to the hospital on the following morning, and as the swelling was not reduced, admission to the hospital was advised.

A general anæsthetic was given, and the external canthus slit. This was rendered necessary by the marked thickening of the lid, and the naturally small palpebral aperture. Upon everting the lid, the enlarged lacrimal gland could be seen as a nodular purple mass projecting downward nearly as far as the edge of the upper lid, but not distended inwards towards the middle line, or downwards below the external tarsal ligament.

An incision was made into the gland substance, and a small quantity of pus evacuated.

On the following day (April 12th) the temperature was normal, and the swelling had subsided to a considerable extent. Three days later the child was discharged.

Flossie O., æt. 21, became O.P. under Mr. Lang, January 26, 1903.

History.—Patient felt a little pain "at the back of the L. eye" 2 weeks ago. There was then a little conjunctival injection.

On January 22nd the upper lid became swollen, hot and tender, but the conjunctiva does not appear to have been

œdematous or shown greater injection than at present time. There was considerable pain. On January 23rd a profuse purulent discharge from the eye began to flow, and the symptoms abated.

There has been no previous attack of inflammation of this or other glands, and no cause can be assigned for this attack.

Present Condition.—The lid is swollen to moderate extent, but the skin shows signs of having been stretched, being now wrinkled and desquamating. There is some tenderness on pressure. The conjunctiva is injected on the outer side, but there is no œdema of this membrane. Upon eversion of the upper lid the lacrimal gland is seen to be enlarged and congested, and pressure of the lid causes pus to exude from a sinus, opening at the most prominent portion of the palpebral part of the gland.

The lacrimal gland of the R. side is normal in size. The L. globe is normal, but the R. globe shows signs of having been severely inflamed at some distant period—probably from ophthalmia neonatorum.

9.ii.03. There is still a little thickening of the lid, and the gland is slightly enlarged. No discharge now.

William V., æt. 34, became O.P. under Mr. Lang, July 28, 1902.

The swelling and pain began 2 days ago.

Present Condition.—Skin over region of L. lacrimal gland is red and swollen.

There is not much pain, but the parts are tender. The lacrimal gland can be felt through the lid as a nodular body, surrounded by indurated tissue. It is easily moved against the frontal bone.

The ocular conjunctiva is injected and œdematous at the outer side, being thrown into folds at the outer canthus. The upper lid cannot be everted, but by gently pulling it forward away from the globe, the inflamed accessory portion of the gland is exposed to view.

Fluctuation cannot be obtained.

28.vii.03. Protruding gland incised, under cocaine, through the conjunctiva. Bead of pus evacuated.

Fomentations every 4 hours ordered.

30.vii.03. Inflammation has subsided: no pain now.

Swelling less marked. Eye is proptosed—proptosis not noted previously.

31.vii.03. Attended hospital. Condition so much improved that further attendance deemed unnecessary.

Arthur B., æt. 37, became O.P. under Mr. Collins on November 3rd, 1902.

History.—A week ago the lids of the L. eye became rapidly swollen and red. There was great pain.

He consulted his doctor, who treated him with hot lotion. The swelling subsided, and the pain was relieved to some extent. Two days later symptoms again developed, more severely than before, and the eye was quite closed by the swelling of the lids.

A gradual improvement then began, with a slight relapse 2 days ago.

A month ago he had an attack of influenza, and was confined to bed for a week, and to the house until a week before the present inflammation.

There is no history of traumatism or constitutional disease.

3.xi.02. The present condition of the patient probably shows a stage of subsidence. The L. upper lid is red, swollen and œdematous. There is much chemosis and injection of the conjunctiva, with a little catarrhal discharge. The lacrimal gland is enlarged and indurated, and manipulation causes a moderate amount of pain.

The pre-auricular and sub-maxillary glands are not swollen.

The globe is normal. There is no displacement or interference with its movements.

6.xi.02. Attended O.P. again. No note made as to condition.

10.xi.02. Swelling less marked, but there is still thickening and tenderness in the region of the lacrimal gland.

13.xi.02. Improvement to such an extent that patient was discharged.

Nelly W., æt. 15, became O.P., May 18, 1903 (Mr. Lang). Slight swelling appeared 14 days ago in outer extremity of L. upper lid. Patient bathed her eye with "boracic lotion and

witch hazel." There was much pain, which continued for several days, but had disappeared at the end of a week. The swelling rapidly increased during first 2 days. She could not open the lids owing to tenderness and stiffness. The conjunctiva was swollen at the outer side. No malaise.

She first attended hospital because she feared a squint might appear owing to the persistent swelling. No history of diplopia.

There has been no preceding affection of the eyes, with the exception of "a slight cold in L. eye, which was watery, but not red." This occurred a week before the onset of the dacryo-adenitis. The R. eye was not watery on that occasion.

There has been no discharge from the eye.

18.v.03. Condition was as follows. Marked swelling of L. accessory lacrimal gland. Upper lid œdematous. Œdema of outer part of ocular conjunctiva, with little increased vascularity. Gland moves freely against the orbital margin. No pain and very little tenderness. Globe moves freely in all directions. No proptosis. It is doubtful whether the posterior limit of the swelling can be distinguished with finger in upper conjunctival fornix, but the indurated tissue becomes thinner as it is traced backwards. R. gland normal.

25.v.03. Upper lid still œdematous. Gland less swollen. No tenderness. Several engorged conjunctival veins at outer canthus.

Patient says that 5 days ago, a "water-blister" developed beneath ocular conjunctiva on outer side. This disappeared yesterday.

4.vi.03. Gland still enlarged. Lid cannot be fully raised.

18.vi.03. Palpebral portion of gland can be felt through lid, and is visible on eversion of lid. No pain or redness.

30.vii.03. No swelling can be now made out. L. upper lid still a little thicker than R. lid. Has pustular blepharitis in R. Does not complain of dryness of L. eye.

The cases described in the literature dealing with this subject divide themselves naturally into two main groups:—

(1) Those in which the affection of the lacrimal gland is associated with mumps. The main features are (*a*) it is usually bilateral; (*b*) suppuration does not occur.

(2) Those in which there is no connection with mumps: the leading features being (*a*) it is usually unilateral; (*b*) suppuration may or may not occur.

In discussing the first group, the writers are agreed upon the course of the disease, but concerning the second, they are strangely at variance. For instance, regarding its characteristic features, Theobald says, "not infrequently both glands are affected," whilst Fuchs only refers to bilateral affection in connection with mumps. Again, in Theobald's opinion, the inflammation very often subsides without the formation of pus, whilst according to Henry Power the condition rarely resolves.

A comparison of the notes shows that this variety of acute dacryo-adenitis has a characteristic form of onset, and runs a definite course, rendering diagnosis easy at all stages. An attack begins with a sensation of stiffness in the outer part of the upper lid. There is some pain and redness, which increase rapidly within the first two or three days. A little conjunctival redness occasionally precedes the onset of the acute symptoms, but in the majority of the cases recorded there was no definite conjunctivitis prior to the inflamed condition of the lid.

The pain, which in the worst cases is severe, is not deep-seated, but is referred to the lid, and in the early stages the patients commonly consider that a stye is forming. This suggests that the palpebral portion of the gland is first involved, the infection spreading backwards to the main part. This feature could, however, be also explained by the swelling of the inflamed structure taking place in the direction of least resistance, &c., towards the front of the orbit. The lid would thus be stretched and the nerves of the conjunctiva pressed upon. A prominent feature frequently at this stage is marked œdema of the ocular conjunctiva on the outer side. This is out of all proportion to the conjunctival inflammation accompanying it, and may be explained by supposing the ophthalmic veins and lymphatics to be pressed upon.

There may be a little catarrhal discharge from the conjunctiva, but it is never profuse.

The lacrimal gland shows distinct enlargement. The surface is nodular, and the vessels lying upon it are seen to be swollen and tortuous, giving the gland a bluish-purple colour. Pressure upon the lid, which causes considerable pain, gives a feeling of general induration of the whole of the outer half of the lid, fading away gradually on the inner side, but being sharply defined on the outer side, being here limited by the external tarsal ligament. This outer limitation is not always visible to the eye, owing to the superficial œdema spreading further downwards.

The temperature of the patient is seldom raised more than a degree, the highest point reached being 100° F. In this particular case the boy was suffering from mumps at the same time. The moderate amount of pyrexia is disproportionate to the extent of the swelling and brawny condition at the orbital margin, and is a valuable means of diagnosis, especially in young children, where the tissues are easily distended, and where it is difficult to make a thorough examination without an anæsthetic. In one case, Jane C., orbital cellulitis was in the first instance suspected, until the temperature was found to be only 97° F.

Malaise to a moderate degree is experienced; it is more marked in the younger patients.

As the disease progresses the eye becomes completely closed, and the upper lid cannot be raised voluntarily. Eversion of the lid is extremely painful, but the gland can be exposed by gently lifting forwards the lid from the globe. It is often covered by the folds of œdematous ocular conjunctiva, which may also obscure the cornea. The skin of the lid becomes stretched and brawny, and it is at this stage that diagnosis is frequently wrong. The condition is taken to be one of abscess of the lid, or periostitis of the orbital margin. An incision through the skin for the relief of the former has failed on two occasions to evacuate pus, which later found an opening through the conjunctiva.

In the early acute stage it is impossible to say whether or not suppuration will take place. The probabilities, however, appear to be in favour of abscess formation, since 8 of the 10 cases here recorded suppurated.

Under an anæsthetic, the gland may be examined by inserting the forefinger into the upper fornix of the conjunctival sac, and palpating the tissues between it and the thumb placed externally. In this way fluctuation can sometimes be obtained. An examination from without to decide the presence of fluctuation is usually futile, owing to the want of resistance of the orbital tissues, and the deep position of the abscess. With the finger in the fornix, the limits of the swelling can be found laterally, but posteriorly it cannot be defined, showing that the palpebral portion of the gland is not alone affected.

Should resolution take place, the pain and swelling abate about the 3rd or 4th day; the lid slackens and can be raised. The conjunctival œdema disappears within 24 or 36 hours, and the malaise is followed by a speedy convalescence. The gland itself, however, although diminishing rapidly in size at first, as the acute symptoms disappear, does not resume its normal dimensions for 2 or 3 weeks.

Should suppuration take place, the symptoms continue, and are aggravated, whilst the physical signs become more marked. The conjunctival swelling is so great that the œdematous membrane may be extruded between the lids, and there retained, causing still greater swelling of the external portion. Even at the height of suppuration the temperature is not much raised.

At a varying period from the onset of the inflammation —from 1 day to a week afterwards—the patient feels the tension of the parts to be relieved. A thick purulent discharge issues from the conjunctival sac simultaneously, and within a few hours there is a marked improvement in the local condition.

The profuse discharge does not last more than 24 hours as a rule. Pus can be seen oozing from the opening in the

gland during this period, but later the discharge diminishes rapidly in amount, and soon becomes little more than catarrhal secretion from the conjunctiva.

Several writers have mentioned that cases of abscess of the lacrimal gland may point externally through the skin of the lid, leading to the formation of a fistula. Indeed, according to Nettleship's text book, "when an abscess forms it usually points to the skin, and should seldom be opened from the conjunctival surface," and Theobald says that "it may make its way to the surface through the integument of the lid, or may discharge into the superior conjunctival *cul-de-sac*." In none of these cases here recorded did the pus appear on the surface, and it is difficult to see why it should do so, since suppuration may proceed much more easily along the gland tissue, and shows no tendency to extend into the neighbouring tissues.

A probe, when introduced through the opening in the gland, passes deeply. The rough walls of the abscess cavity can be felt, but the wall of the orbit does not appear to be affected in any way, and is certainly not exposed.

Bock, in an exhaustive article on this disease, states that the accessory gland is not always involved, or, if involved, is not affected to a similar degree, whilst Nettleship, as before-mentioned, has met with cases of affection of the accessory portion alone.

Bock's observation cannot be substantiated from the above cases. In all of them, where an abscess formed, the two portions of the gland appeared to be matted together, the anterior part of the mass being distended downwards almost to the margin of the upper lid. In one instance of probable affection of the accessory gland due to extension of the inflammation of a suppurating Meibomian gland, which had discharged through the skin near the external canthus, the finger in the upper fornix could make out the posterior limit of the involved tissue. There was no evidence of affection of the deep gland, or of pus formation in the accessory portion. The fact that in several of those cases

operated upon, about a drachm of pus was evacuated, suggests that the greater part of the gland tissue was destroyed, the only healthy tissue being a thin shell forming the abscess wall. There was no reason to believe in any single case that the suppurative process was not wholly limited to the gland tissue.

Both during the height of the disease, and in the later stages, it was impossible to say whether or not the function of the gland was in abeyance. In most of the cases there was a little catarrhal discharge from the conjunctival sac, but there was certainly not an excessive amount of tear secretion. The secretion from the conjunctiva was sufficient for the purposes of lubrication, and, notwithstanding the heat of the parts, and probable desquamation of the conjunctival epithelium, dryness of the eye was not complained of at any stage.

The intensity of the inflammation, and the breaking down of gland tissue in some cases, would lead one to expect complete atrophy subsequently, but this was not observed in this series. The accessory portion can be exposed many months afterwards, and no difference can be detected between those of the two sides. Of course, the gland tissue must largely be replaced by fibrous tissue, and it may be the fibrous remains which are exposed to view on everting the lid, and the absence of any dry sensation of the eye due to abolition of tear secretion would not be surprising, since the lacrimal gland can be completely extirpated without any apparent want of moisture following its removal.

It is curious that the swelling of the main part of the gland was not observed to cause displacement of the globe, or to interfere in any way with the movements of the eye. Bock relates that one of his cases, and five of those recorded by Von Reuss, showed no displacement of the globe; in the others it was pushed downwards and inwards.

In one of the cases, William V., recorded above, proptosis was noted 2 days after the abscess had been opened. This was not observed before the operation; it was only

slight, and cannot be explained, since the swelling of the tissues had subsided to a considerable extent.

Even if mechanical displacement did not occur, it is difficult to see why Tenon's capsule should not become affected by the neighbouring inflammation. There was no sign of this complication. The eye could be rotated in all directions quite freely without causing any pain, and abduction appeared to be as easy as any other movement, showing the external rectus to be not involved.

When the height of the inflammation has been passed, the elevator of the upper lid soon resumes its full action, but for some weeks afterwards there is some fulness of the upper lid in its outer half, causing a convexity of the palpebral margin, which gives the patient an appearance of winking.

The gland itself may remain enlarged for a period of a month or 6 weeks afterwards.

Of the 10 cases observed, 6 occurred in males and 4 in females. Several cases other than those above described have come under notice during the past 2 years, but are not included in this series on account of their course not having been closely followed. In all of these, the sexes appeared to be equally affected. The age at which the disease may be expected shows wide limits. In Bock's investigations the earliest age was 8, and the latest 77 years. In the present series, there were 3 patients of the ages of 3, 4½ and 6 years respectively, whilst the oldest individual was 37.

That it is an affection of youth is indicated by the average age being 16, and acute inflammation is certainly more severe in the young patients.

The left side is much more frequently attacked than the right side, 9 of the 10 cases being on the left. No cause can be assigned for this marked difference.

Several writers have commented upon the association of dacryo-adenitis with swelling of the parotid gland, and

Bock, discussing the causation of the disease, suggests that some of these cases may be mumps of the lacrimal gland, the latter being only a modified salivary gland. He adds that the swelling of the parotid is especially noticeable in sub-acute and chronic cases.

Lawson states that a case of bilateral sub-acute inflammation of the lacrimal glands under his care seemed in its course to be very analogous to an attack of mumps, although there does not appear to have been any involvement of the salivary glands.

In only one instance of the present series was this interesting complication present. The affection of the salivary gland preceded the dacryo-adenitis by only 24 hours. The glands of the opposite side were normal throughout the course of the disease. Suppuration occurred in the lacrimal gland, but not in the salivary gland. According to Osler, suppuration is "an extremely rare complication in genuine idiopathic mumps." Yet in the only case occurring during an attack of mumps, an abscess formed, and was evacuated.

This circumstance makes it difficult to decide into which of the two groups before mentioned this case should go. Although associated with mumps, there was present neither of the characteristic features which seem to distinguish it as one of the first group, and the fact that the lacrimal gland suppurated whilst the parotid resolved in the usual manner, suggests that the lacrimal disease was merely coincident with the parotitis, a different form of infection having taken place.

In reviewing the cases under notice, one is forced to the conclusion that in every instance the disease was a purely local condition, as the symptoms disappeared rapidly as soon as the pent-up pus had free outlet.

With regard to the entrance of pyogenic or other organisms, attention may be drawn to the impetigo of the nostrils, and the blepharitis from which Jane C. and Leslie F. respectively suffered on admission to the hospital, and

to the severe phlyctenular conjunctivitis and pustular blepharitis which subsequently developed in Jack D. and Nellie W. In the latter two cases it might be argued that the conjunctiva was infected secondarily, but a sufficient time had elapsed in each instance for the whole inflammatory attack to have subsided, and both patients had been seen in a normal condition in the interval. There was no relapse of the dacryo-adenitis.

The lacrimal sac was invariably healthy in the series.

Bock lays stress upon the acute infectious diseases as precursors of the suppurative form. This cannot be substantiated from these cases, as there was no history of immediately preceding illness. In one child, of about 3 years, however, whose notes cannot be unfortunately traced, an attack of measles had occurred rather more than a fortnight previously, and the inflammation ended in the formation of an abscess.

The diagnosis of acute dacryo-adenitis presents little difficulty. When the inflammation is at its height, the closure of the palpebral aperture, the chemosis of the conjunctiva, and the great swelling of the tissues of the lid, have led to a diagnosis of orbital cellulitis. But, notwithstanding the tenderness of the parts, an examination of the upper lid soon demonstrates that the induration is confined to the outer part, the rest of the lid being swollen in a more or less passive manner. The fact that the lid cannot be everted at this stage without much difficulty and pain accounts for the prominence and congestion of the gland remaining unobserved, whilst the marked œdema of the conjunctiva, which may entirely obscure the cornea, give an impression that the globe is involved. The comparatively mild constitutional disturbance, moderate pyrexia, and absence of ocular symptoms, help to a correct conclusion as to the nature of the case. Examination of the upper fornix, under a local or general anæsthetic, according to the age of the patient, is conclusive.

Periostitis of the orbital margin has been suggested in

moderately severe cases. In such instances a sulcus could always be felt with the tip of the finger, between the point of greatest swelling and the rim of the orbit, and once, where tenderness was not a marked feature, the swollen gland could be moved freely against the bone.

The treatment of acute dacryo-adenitis is simple, and consists of hot fomentations applied frequently to the part. Theobald advocates "leeching, and the liberal application of an ointment of mercury and opium or belladonna, together with the administration of an energetic calomel cathartic, to be followed by free doses of quinine, salicylate of sodium, or pyrophosphate of sodium." This, it is hoped, would cut short the attack. If ineffectual "poultices or warm fomentations are to be applied, and, as soon as the presence of pus can be detected, it should be evacuated by a free incision, made either through the integument of the upper lid, or from the conjunctival *cul-de-sac*, as may seem to be indicated by the tendency of the abscess to point."

Concerning the treatment adopted in dealing with the cases recorded the latter part of this scheme was practically carried out, but no attempt was made to cause the condition to abort, since in the non-suppurative inflammations amelioration of the symptoms was obtained at once by the application of moist heat. Where pus is present, or, rather, where the severity of the symptoms and the extent of the swelling justify the assumption that an abscess exists (for fluctuation cannot always be obtained), an incision should be made, but never through the skin. The disadvantages of the latter method are the production of a scar, and the possible formation of a lacrimal fistula. But, as far as one can judge, it is never necessary, as the abscess tends naturally to discharge itself into the conjunctival sac.

The procedure adopted was to anæsthetise the patient if young, evert the lid if possible, and, by pressure at the orbital margin, force the gland to present. It was then incised with a Beers' knife, and, if pus did not appear, a pair of sinus forceps was introduced, and the aperture enlarged

In the youngest patients it was found necessary to slit the external canthus in order to get a good view of the structures behind the lid.

Fomentations were then applied, and recovery quickly followed. Whilst the discharge was profuse, boracic acid ointment was used to protect the cornea, and the conjunctival sac was frequently irrigated. Constitutional treatment was never needed.

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